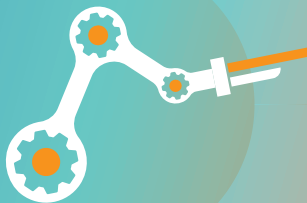


PENN Medicine



PUTTING DISCOVERIES TO WORK

A growing list of FDA-approved
therapies is rooted in
research at Penn Medicine.



Plus:

The New Science of Cancer Interception

Students Gather at the Nexus of Medicine, Tech, and Business



Benjamin, Lucy, and Erin Prosser

CLOSE TO HOME

In 2018, Benjamin Prosser, PhD, was more than a decade into a promising career studying heart failure. After his daughter, Lucy, was born that year and diagnosed with a rare genetic disorder called *STXBPI* encephalopathy, he drew a new map for his work. He threw himself into researching her condition, which is tied to epilepsy and neurodevelopmental delays. Now, with a \$25 million gift from an anonymous donor, Prosser, an associate professor of Physiology in the Perelman School of Medicine, is set to expedite efforts to find new treatments for kids like Lucy through a collaboration with Children's Hospital of Philadelphia (CHOP) colleagues Beverly Davidson, PhD, and Ingo Helbig, MD, to form the Center for Epilepsy and Neurodevelopmental Disorders (ENDD).

ENDD will initially focus on developing therapies for disorders related to mutations of the *STXBPI* and *SYNGAP1* genes with the goal of expanding its efforts to other genetic neurodevelopmental disorders over time.

"As a scientist and as a parent, I am incredibly grateful for this gift, which will propel our work forward with the hope of changing the course of these disorders," Prosser said. "We have a rare opportunity with such a brilliant and dedicated team of scientists and clinicians at Penn and CHOP, who are motivated each day to make a difference for Lucy and children like her."



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PENNMEDICINE

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14 Making What's Next in Medicine *By Karen L. Brooks*
Since 2017, the FDA has approved more than two dozen new therapies with roots at Penn Medicine — almost half of which are first-in-class for their indications. Becoming a hub for drug research and development took a lot more than luck.

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By Kirsten Weir
Penn researchers hope to change the game by interrupting the development of more types of cancer at their earliest stages.

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PennHealthX has grown over 10 years as an influential student-driven creative hub for projects and programs at the intersection of medicine with other disciplines.

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Serving a Changing World

Penn Medicine is the place that made a whole new type of vaccines possible by harnessing the power of mRNA. It's also the place that first cured cancer by re-engineering patients' own immune cells to conquer their disease. And Penn Medicine is the place where the first gene therapy became an approved treatment, reversing an inherited form of blindness. All of these banner discoveries took decades of effort for novel ideas to become clinical treatments making a difference for patients, and they are among countless other stakes planted in the ground here. Dozens of new treatments and cures, in just the past few years, are rooted at Penn.

That it all happened here is more than just luck. Whether recruiting and promoting the right people, or smoothing processes associated with clinical research and developing intellectual property, Penn Medicine's leaders have deliberately invested in making this a place where we create new medicines that the world needs — as detailed in this issue's cover story (p. 14). The next generation of innovation is well underway, as our researchers define an entirely new field that could intercept cancer cells at the earliest phases and forestall the disease altogether (see p. 26).

In short, Penn Medicine is a place where we *make breathtaking discoveries and put them to work*.

That phrase is both a directive and a guiding principle. In fact, it's one of five guiding pillars for Penn Medicine's new strategic planning process that is in progress this academic year. The five pillars derive from the organization's core missions that our faculty and staff work to advance every day. But these pillars also refocus our community with specific goals in mind. The research mission isn't solely about discovery for the sake of knowledge or intrigue. *Breathtaking discoveries* push the boundaries of what we thought possible — and putting them to work means we push for those discoveries to change the world for the better.

As another example: Penn Medicine's educational mission is about more than just conferring degrees, which is why the charge is instead to *develop people for great accomplishment*. Medical students come to the Perelman School of Medicine to learn and grow in an environment that supports them as they flourish along paths of their own design — as with the student-initiated PennHealthX group that for 10 years has created learning opportunities at the intersection of medicine, business, and technology (see feature story, p. 30). The strategic planning process asks us to consider, what more can we do to make Penn Medicine a place where people grow for great accomplishment — in the classroom, in clinical training, and in the professional workforce?

Similar questions and aspirations follow across the remaining three pillars: Making care easy and putting it within reach;



uplifting our community, our environment, and ourselves; and leading with humanity in all that we do.

Every decade of Penn Medicine's long history tells the story of our commitment to these principles. Now, hundreds of faculty and leaders from across the organization are working together to plan how we will take that work forward for the next five years as the world is changing all around us.

Since the last time the organization undertook a strategic planning process, in 2017, the COVID-19 pandemic upended the way health care had been delivered for generations, reshaped the economic forces that propel research and improvements in patient care, and shifted countless aspects of the wider society in which Penn Medicine exists. The challenges have grown more acute and more urgent in areas from racial health inequity to climate change to the cost of health care.

That state of change is an impetus and a source of momentum for the work that lies ahead, according to J. Larry Jameson, MD, PhD, executive vice dean of the University of Pennsylvania for the Health System and dean of the Perelman School of Medicine. The fundamental question is, "What does the world need from Penn Medicine and how can we deliver it?"

"Let's be even bolder now," he said, in kicking off the planning process this December. "It is time for us to embrace the opportunity for Penn Medicine to shape what we can do in the world."

RE

Rachel.Ewing@penmedicine.upenn.edu



For the 126 students who matched, the long, nerve-racking wait was over, as they discovered the destination for their next few years of training. Nearly one-third of the class matched to a Penn program. Natalia Rodriguez (at left with Dean Rose) will be pursuing Dermatology at Penn, while Canada Montgomery (above) will continue her training here to become one of the country's few female Black neurosurgeons.



Overall, 98.5% of students matched (above the national average of 93%), and 38% will be heading to a primary care residency (Family Medicine, Internal Medicine, Pediatrics, or combined Internal Medicine/Pediatrics) like Matthew Barrett, who will be heading to New York Presbyterian Hospital/Columbia University Medical Center for a residency in Internal Medicine.

THE MATCH GAME

"Welcome to your future!" With those words, Perelman School of Medicine Senior Vice Dean for Medical Education Suzanne Rose, MD, MSEd, congratulated the medical students in their final year who were about to open envelopes which told them where they matched for residency.

Match Day 2023 was especially festive. That's because, after three years of COVID-19 restrictions, full cohorts of family and friends were finally invited back in to the Jordan Medical Education Center to share the moment with their budding soon-to-be-physicians.

Alluding to Match Day's confluence with St. Patrick's Day this year, Rose also shared a message from PSOM Dean J. Larry Jameson, MD, PhD, who was watching the event remotely due to a recent COVID exposure: "I'm holding a four-leaf clover for each of you!"

► [Read more and watch a video from this year's Match Day at PennMedicine.org/news/news-blog](https://www.pennmedicine.org/news/news-blog)

SEEING PENN THROUGH NEW EYES



Bennie H. Jeng, MD

A return to Penn brings new beginnings for the new chair of the Department of Ophthalmology and director of the Scheie Eye Institute.

For Bennie H. Jeng, MD'98, the perspective he has on returning to Penn Medicine to lead the Department of Ophthalmology and the Scheie Eye Institute last year, nearly a quarter century after graduating from the Perelman School of Medicine, can be summed up in a single encounter from his student days.

Jeng and his eventual wife, Linda (Bone) Jeng, MD/PhD'98, were seated together with then-department chair Stuart Fine, MD, in the same office that Jeng now occupies. "Stuart wanted to make sure we fully understood the intricacies of the couples matching process," he says. "To have a department chair — especially one of Stuart's stature — be so focused on a student's future success made a huge impression on me."

That experience still informs Jeng's approach to leadership now. "When students know someone cares about them, it can really make a difference in their lives," he says.

Leadership by Example and Evolution

His Penn position isn't Jeng's first one as a department chair. When he took on that role at the Department of Ophthalmology and Visual Sciences at the University of Maryland School of Medicine nearly a decade ago, a mentor cautioned him that, as a department chair, everyone else's priority becomes your priority. "I have found that to be true up to a point," Jeng says. "But luckily my priority is to mentor people to help them excel, from faculty, to fellows, to residents, to students, so that works out well."

In July 2022, he assumed his current role at Penn, which also includes serving as director of the Center for Translational Bioinformatics and associate director of the Penn Center for Precision Medicine.

For Jeng, leadership means doing what he asks of others. "I lead by example with full transparency and fairness," he says. For example, he still keeps an active clinic schedule, takes his turn responding to trauma calls in the Emergency Department, and maintains his independent research program.

"How can I ask my faculty to do more of all these things if I'm not doing them myself?" Jeng asks. "I hope my energy has brought a fresh view of the department to the faculty as a whole."

Assuming the directorship of the Scheie Eye Institute in its 50th anniversary year Jeng is both proud to celebrate the milestone and attuned to a changing landscape for the department. In medical education, he embraces the more active learning style of today's medical students and trainees. "Our educational approach is now more conversational and focused on critical thinking and asking and answering questions," he says. In research, Jeng says the department is refocusing its basic science program, especially focusing on optical tissue degeneration and ultimately regeneration of the optic nerve and the retina. Additionally, he envisions the department increasing its clinical trials portfolio and growing the geographic reach of its clinical practices.

A Passion for Improving Global Eye Health

A nationally recognized clinician-scientist specializing in cornea and external eye diseases, Jeng was initially drawn to transplant medicine before finding a fit in ophthalmology. "I wanted to be involved with the longitudinal care of patients and pursue a field where I could do research but also have a major impact on patients' lives," he says. "Focusing on corneal transplants combines all of my interests."

In corneal transplantation, surgeons replace the clear, domed surface of the eye with tissue from a donor. Eye banks, the institutions that obtain, evaluate, and distribute donated tissue, are another area of expertise for Jeng. "Eye banking is well-developed in the U.S. but not everywhere," he explains. "Developing educational resources and infrastructure is very important in the global fight against corneal blindness."

For this reason, Jeng does not do conventional mission trips, preferring instead to focus on training local surgeons. "I don't want to go, operate on dozens of patients, and then leave them with someone who is not trained in proper follow-up care," he says. "It's the old story about teaching someone to fish for themselves versus just giving them a fish for a single meal."

— Darcy Lewis



PENN MEDICINE AND WHARTON INVEST FOR PUBLIC HEALTH IMPACT

How can a health system meaningfully improve a community's health when many of the underlying causes of illness trace to social factors — economic disadvantage, lack of access to primary and specialty care, food insecurity, and more? Investing in startup businesses is one of the newest ways Penn is answering that call to serve the community's health needs.

Penn Medicine and the ESG Initiative at the Wharton School created the Fund for Health with a \$5 million initial investment in 2021. Philanthropists Josh Harris, managing partner of the Philadelphia 76ers, and his wife, Marjorie Harris, announced that they would invest up to an additional \$1 million in companies funded by the program. Since inception, the Fund for Health has invested \$1.6 million in early-stage businesses striving to strengthen the social determinants of health affecting underserved Philadelphians.

For the initiative, a diverse investment team of students from across the University of Pennsylvania, including from

the Wharton School and the Perelman School of Medicine, is tasked with sourcing and conducting due diligence on early stage, for-profit companies set out to strengthen social determinants of health. The team of students has grown from an initial cohort of 6 to a total of 16 to date. Demand for the program is high, with over 70 applicants per year. Two of these student associates, third-year medical students Medha Sharma and Michael Karamardian, went on to co-found the PennHealthX Social Determinants of Health Accelerator program (see p. 30).

"We are proud of the collaboration with Penn Medicine which created the Fund for Health, which provides a hands-on opportunity for students to gain knowledge and experience in impact investing," said Witold Henisz, vice dean and faculty director of the ESG Initiative.

These companies have received Fund for Health investments to date:



Kinolved, communications software to reduce absenteeism in underserved school districts.



Uprust, a tool that helps keep people out of the criminal justice system by avoiding unnecessary technical violations, like missing court dates or probation appointments.



RecoveryLink, a telehealth and electronic records platform that improves recovery support services to people experiencing substance use and mental health disorders.



Fabric Health, a Philadelphia-based startup that partners with health insurance companies to provide health screenings and preventive care through laundromats.



Stimulus, a Philadelphia-based service that helps business teams collaborate to choose the right suppliers and achieve their DEI purchasing goals.



Lula, which provides a platform and support for small, often family-owned convenience stores and pharmacies to deliver to customers via apps like DoorDash, Grubhub, and Uber EATS.



Twentyeight Health, an online platform and telemedicine service designed to expand reproductive health care access for women from underserved communities.

"The challenge of achieving health equity is too important not to try every tool in our toolbox and put all of our great minds toward the task," said Kevin B. Mahoney, CEO of the University of Pennsylvania Health System. "Making investments in innovative small businesses has the potential to make an impact in both the health and economic well-being of Philadelphians, and communities in need across the country."

UNITING AGAINST AUTOIMMUNE DISEASE



From left: Jonathan Epstein, MD, executive vice dean and chief scientific officer, Perelman School of Medicine (PSOM); Ezekiel Emanuel, MD, PhD, vice provost for Global Initiatives, University of Pennsylvania; J. Larry Jameson, MD, PhD, dean, PSOM; Penn President Liz Magill; Judy Colton and Stewart Colton; E. John Wherry, PhD; and Kevin Mahoney, CEO, University of Pennsylvania Health System.

An additional \$50 million commitment from Judy and Stewart Colton, W'62, to the Colton Center for Autoimmunity at the Perelman School of Medicine is set to accelerate leading-edge research efforts towards prevention and treatment of diseases like Type 1 diabetes, celiac disease, multiple sclerosis, and rheumatoid arthritis. This gift builds on a \$10 million gift establishing the center at Penn in the fall of 2021 as part of a consortium of centers which includes New York University, Yale, and Tel Aviv University.

The new gift provides resources for the Colton Center at Penn to build a world-class home for autoimmune research co-located with immune health, vaccinology, virology and viral immunity, SARS-CoV-2 research, fundamental immunology, and related areas.

Additional priorities for the center include creating powerful recruitment capabilities; further development of Penn's Immune Health platform; provision of both internal and external grants to fund promising ideas; initiation of adaptive clinical trials; and expansion of artificial intelligence and big data. In the coming years, Penn envisions multiple avenues of connection to the other centers, including retreats and

scientific meetings, collaboration between leadership and faculty of the four centers, and the development of multiple scientific initiatives.

"The Coltons' vote of confidence in our approach and additional investment means the Center at Penn will be able to better unite researchers, physicians, entrepreneurs, and more — not just across Penn but around the world," says Colton Center Director E. John Wherry, PhD, the Richard and Barbara Schiffrin President's Distinguished Professor, chair of Systems Pharmacology and Translational Therapeutics, and director of the Penn Institute for Immunology & Immune Health. "The goal of the Colton Consortium is to leverage complementary strengths at each institution and, by embracing this collaboration, we can accomplish so much more than any one lab or site alone. Together, we make up a tremendous center of gravity for autoimmune research and innovation."

► **Learn more about Judy and Stewart Colton in "Development Matters" from the Spring/Summer 2022 issue of *Penn Medicine* magazine.**

A PORT IN THE STORM

Penn Medicine is leading the quest to understand and treat a deadly cytokine condition.

In the distance, the storm appears relatively benign: fatigue and abdominal pain. Then come the night sweats and fevers. As the storm gains strength, the pain and fatigue become unbearable. The lymph nodes enlarge. In its full fury, the storm wreaks havoc on everything it touches.

It's the chilling reality of a cytokine storm, the powerful and mysterious autoimmune condition with several known causes and precious few treatment options. In a functional immune system, the cytokine protein promotes healthy inflammation in response to infection, trauma, cancer, and similar problems in the body. But in a cytokine storm, also known as cytokine release syndrome, the body floods itself with an extreme amount of these molecules, leading to a wide range of symptoms, serious organ damage and, if left untreated, death.

Once considered uncommon, cytokine storms gained new notoriety as a deadly complication of COVID-19. As a result, interest in cytokine storms has increased. Penn Medicine has emerged as a leader in cytokine storm research.

"It feels like the worst flu you've ever had, and on top of that, your organs start to shut down," said David Fajgenbaum, MD'13, MBA'15, MSc, a nationally renowned cytokine storm researcher and an assistant professor of Translational Medicine and Human Genetics at the Perelman School of Medicine at the University of Pennsylvania. "Your liver, kidneys, heart, and lungs all can shut down, because your immune system is out of control. You either die or you hit the immune system with the right drug at the right time to stop it. Relatively speaking, we really don't know very much about them."

Fajgenbaum knows of what he speaks. In 2010, he was diagnosed with idiopathic multicentric Castleman disease, a rare affliction that causes cytokine storms. Fajgenbaum has been admitted to the ICU five times for the condition.

Breakthrough discoveries from Penn Medicine have advanced scientific and clinical knowledge of cytokine storms. Most recently, a study led by Fajgenbaum and published in *Nature Communications* revealed that a protein called CXCL13 could serve as a biomarker to help better predict a patient's response — or dangerous lack thereof — to siltuximab, one of the few Castleman treatments on the market today.

"I hope this research helps clinicians treat patients like me more effectively," Fajgenbaum said. "This test could lead to more effective treatment approaches. We're helping improve the speed and accuracy of diagnosis and uncover new treatment approaches that save lives."



Penn Medicine's history with cytokine storm research traces back more than a decade. In 2012, a cytokine storm nearly killed 6-year-old Emily Whitehead, the first pediatric participant in a trial investigating CAR T-cell therapy developed at Penn Medicine and Children's Hospital of Philadelphia. It was thanks to quick thinking by CAR-T pioneer Carl June, MD, that doctors saved her life using the arthritis drug tocilizumab. That drug was subsequently approved by the U.S. Food and Drug Administration for treating cytokine storms in people undergoing CAR T-cell therapy, along with the landmark approval of the CAR-T therapy itself, in 2017.

Fast forward to the COVID-19 pandemic, when many infected patients experienced cytokine storms to devastating effects. Fajgenbaum and June developed a unifying definition of cytokine storm to guide clinicians, published in the *New England Journal of Medicine* in December 2020. A 2022 literature review in the journal *Virology* concluded that cytokine storms are "one of the possible events for the progressive and severe forms of COVID-19 and its mortality," and that "management of the cytokine release syndrome... may be an intriguing approach for COVID-19 therapy."

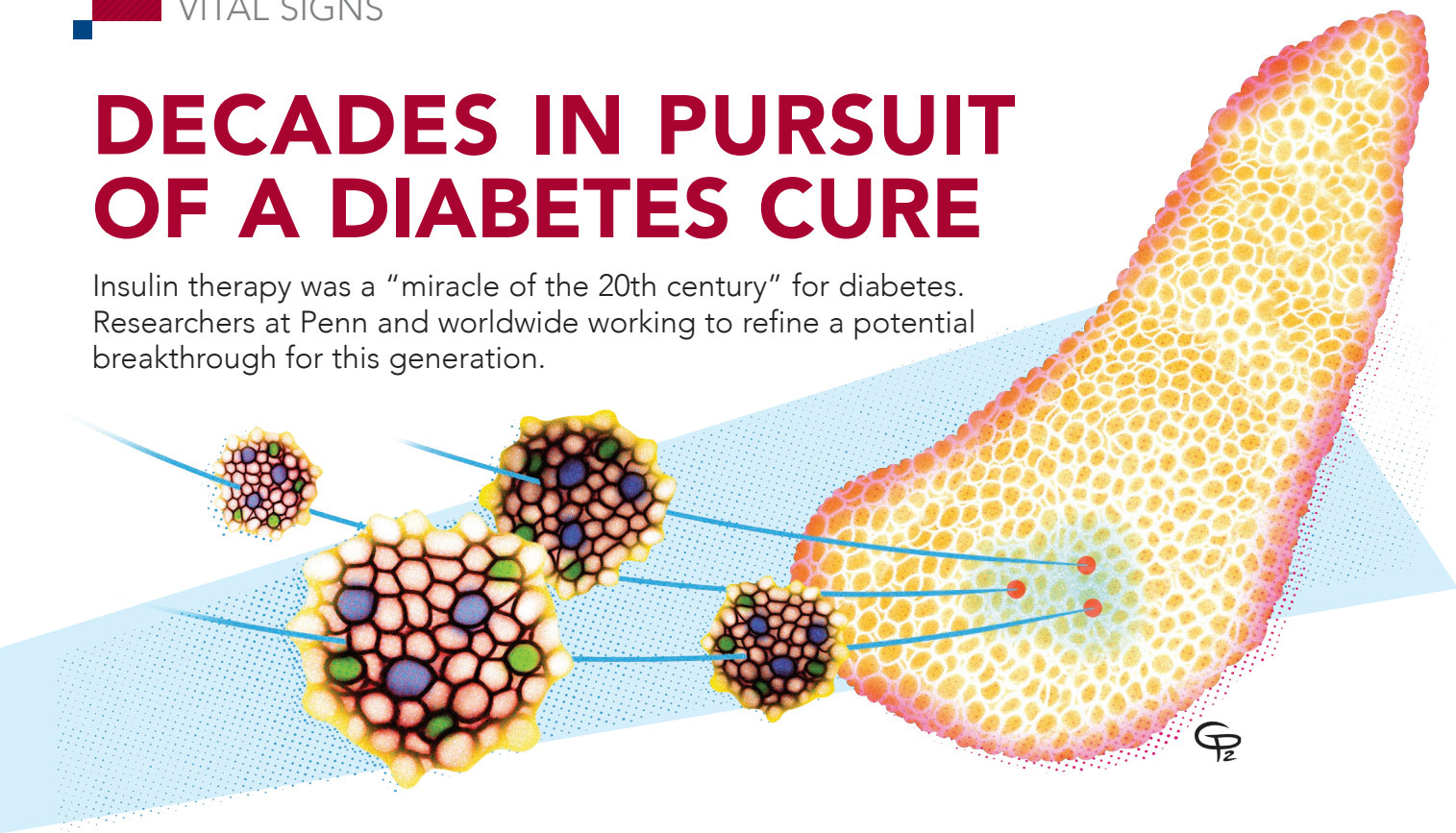
This is a driving factor behind the work underway at Penn's Center for Cytokine Storm Treatment and Laboratory, which Fajgenbaum founded. Fajgenbaum also founded the Castleman Disease Collaborative Network, which connects thousands of Castleman clinicians, researchers, and patients around the country.

The next big goal of Penn Medicine's cytokine storm research: more diagnostics advances. The ultimate objective is safe harbor for everyone at risk.

"We need to implement the biomarker test to inform personalized treatment of patients," Fajgenbaum said. "We have a lot more work to do." — Scott Harris

DECADES IN PURSUIT OF A DIABETES CURE

Insulin therapy was a “miracle of the 20th century” for diabetes. Researchers at Penn and worldwide working to refine a potential breakthrough for this generation.



The patient had a full life: She held a demanding academic post, and was raising young children. She took shots of insulin regularly to manage her Type 1 diabetes. Even so, she couldn't always tell when her blood sugar dipped dangerously low. Without realizing it, she'd find herself in hypoglycemic shock — her thinking impaired, her movements clumsy. If she didn't recognize what was happening in time, she could even pass out or experience a seizure.

“It was so disruptive at every level of her life,” recalled Ali Naji, MD, PhD’81. “It’s a life-threatening situation.”

In 2009, the woman became a participant in a trial Naji led to transplant islet cells isolated from a donor’s pancreas to her own liver. A narrow catheter delivered the donor cells to the portal vein leading to her liver, where they began to thrive.

Today, 14 years later, Naji’s patient no longer experiences hypoglycemia. What’s more, she no longer needs to take insulin — a result that held true for more than half of the other patients in the trial.

It’s an outcome that may someday be common in the U.S., and is part of a global project to find better treatments for Type 1 diabetes — a project to which Naji has dedicated decades of his career at Penn.

Intelligent Control

Naji first started working on diabetes as an immunology PhD student at Penn in the 1970s. Naji was already a medical school graduate, but, he says, “When I finished my training as a general surgeon, I really thought that I needed to acquire in-depth basic science if I wanted to compete in an academic setting.” His studies led him to work beside the pioneering

transplant surgeon and founder of Penn’s transplant program, Clyde F. Barker, MD.

Barker knew first-hand how devastating diabetes could be from performing amputations on patients after the disease had caused neuropathy and blood vessel loss in their limbs, and from performing kidney transplants for people whose diabetes had damaged their own. “Both Barker and I knew that diabetes is a really disastrous disease,” Naji said.

At the time, it had been about 60 years since the advent of insulin therapy had changed diabetes from a fatal disease to a chronic one — “one of the miracles of the 20th century,” Naji says.

But even modern insulin therapy can’t replicate the way the body naturally regulates its insulin levels to control blood glucose concentrations in the normal range. That takes place in tiny clumps of cells scattered throughout the pancreas like so many islands — which are therefore known as “islet cells.”

Some of the cells in these clumps, beta cells, produce insulin, the hormone that helps all the body’s cells take in the glucose they need to function. “It’s an amazing metabolic control, very precise,” said Naji. Governed by the enzyme glucokinase, discovered at Penn by the late Franz Matschinsky, MD, beta cells are capable of sensing and responding to minute changes in the amount of glucose in the bloodstream, making more or less insulin accordingly.

“They are really intelligent,” Naji said. “They have the best radar system that God almighty has ever put in our cells.”

In Type 1 diabetes, these cells are attacked and destroyed by the body’s own immune system, a paradigm that Naji helped to establish. Regular injections or continuous infusion

of insulin compensate enough to keep a patient alive — but compared to the precisely calibrated, real-time responses of islet cells, dumping a set amount of insulin under the skin that must make its way into the bloodstream is a blunt method. That’s why patients may still experience severe long-term effects of diabetes even with insulin treatment: blindness, circulation problems, nerve damage, kidney failure, stroke, seizures — and, of course, hypoglycemic attacks.

‘Simple but Practical’

Transplanting an entire healthy pancreas can help patients produce and precisely regulate insulin on their own, but the surgery is dangerous, invasive, and complicated. Barker wondered whether transplanting just the islet cells could be just as effective. “He always believed in simple but practical approaches,” Naji recalled.

When Naji began studying with him, Barker was working on animal studies. “It was really amazing as a graduate student to cure an animal [of diabetes] with a simple injection of islet cells,” Naji recalled.

It took decades for Barker and other medical scientists pursuing the idea to learn how best to successfully isolate human islet cells, and to determine how best to transplant them into people.

Over the years there were sporadic, experimental islet cell transplants around the world, but in 2000 a Canadian team successfully performed seven such procedures in a row.

Naji wanted to replicate that success. “I went to Barker and said, ‘It’s time to expand this novel therapy for human clinical trials,’” he recalled.

To isolate islet cells for human transplantation, Naji needed a special, million-dollar facility. Barker found space for him at Stemmler Hall, and philanthropic contributions helped him create a “small but efficient” lab in 2000 where he could process donor pancreases into islet cells ready for transplant.

In 2004, the National Institutes of Health formed the Clinical Islet Transplantation Consortium, a network comprising investigators from across the country as well as Canada and Sweden. Naji and Penn were among them. Over the years, Naji and Penn colleagues including Michael Rickels, MD’99, now the Willard and Rhoda Ware Professor in Diabetes and Metabolic Diseases, worked to improve and standardize methods for islet isolation and transplantation, with techniques that include manipulating the immune system to prevent rejection and designing therapies to prevent the islet cells from being damaged or stressed after transplant. A Penn endocrinology fellow at the time, Naji conducted the first islet cell transplant in a patient at the Hospital of the University of Pennsylvania. Rickels investigated how the transplanted islets functioned in their new home of the liver, both to release insulin as well as the islet hormone glucagon that is impaired in type 1 diabetes and critical to the counterregulatory defense against the development of hypoglycemia.

Recently, Rickels led the Consortium’s follow up of the patients who received islet cell transplants as part of the National Institutes of Health–sponsored phase III clinical trials, including those isolated in Naji’s lab. Eight years later, Rickels wrote, over 90% remained cured of their hypoglycemia, and 74% achieved a period of insulin-independence, with more than half no longer requiring insulin.

Building a Better Drug

While islet transplantation has become a standard treatment in the U.K., Canada, Europe, and Australia, in the U.S., federal regulations classify isolated islet cells as a drug, not an organ transplant. This makes the procedure of isolating islet cells prohibitively expensive to perform for commercial production under biologic licensure required by the FDA. So the procedure is in limbo: Despite successful phase III clinical trials, only very limited research support is available in the U.S. But without an industry partner, none of the academic medical centers that manufactured islets for the trials has achieved the FDA licensure required to offer islet cell transplantation in clinical practice.



Ali Naji, MD, PhD

Meanwhile, research has continued. In addition to his ongoing practice as a transplant surgeon, Naji, together with Rickels, is now leading trials based on discoveries by a researcher at Harvard

University, Douglas Melton, PhD, who aims to make islet transplantation even more effective. Instead of isolating islet cells from donor organs, Melton has been growing them from stem cells. These stem cell–derived islets are now being transplanted in a phase I/II clinical trial using the liver as a transplant site and immunosuppression as established by Naji and Rickels as part of the NIH Consortium for deceased donor islet transplantation. Other investigators in the lab are using the gene-editing technology of CRISPR to make these stem cell–derived islets invisible to the recipient’s immune system. This may eliminate the need for future islet cell transplant recipients to take immunosuppressant anti-rejection drugs.

Melton is also developing a procedure for implanting the cells just beneath the skin, rather than in the liver — a less invasive approach. “I am delighted by the progress of science,” Naji said. “It is a really exciting time — I really believe we will have enormous opportunity to cure Type 1 diabetes.”

— S.I. Rosenbaum

A POLICY PUSH FOR HEALTH EQUITY



Between 2017 and 2023, the number of non-binary patients in the Penn Medicine system increased from 14 to more than 4,000.

The reason? Providers simply started asking patients about their gender identity, along with better documenting patients' sexual orientation and racial and ethnic backgrounds with new fields in the electronic medical record.

"It's a technical, behind-the-curtain fix, but it has such meaning," said Jaya Aysola, MD, MPH, "because you're identifying people who were never recognized before in your organization, and for the first time these patients are feeling seen within their health care system."



Executive Director Jaya Aysola, MD, MPH, founded the Center for Health Equity Advancement within the office of Penn Medicine's Chief Medical Officer PJ Brennan, MD.

Aysola is the founder and executive director of Penn Medicine's Center for Health Equity Advancement (CHEA). Through CHEA, she has led efforts to bring greater equity to the health system since 2015 — years before equity and inclusion became buzzwords in health care.

When a greater number of leaders across the country began to address the challenge of racial and ethnic health disparities in 2020, Aysola answered the call to share her expertise and advance equity at the policy level.

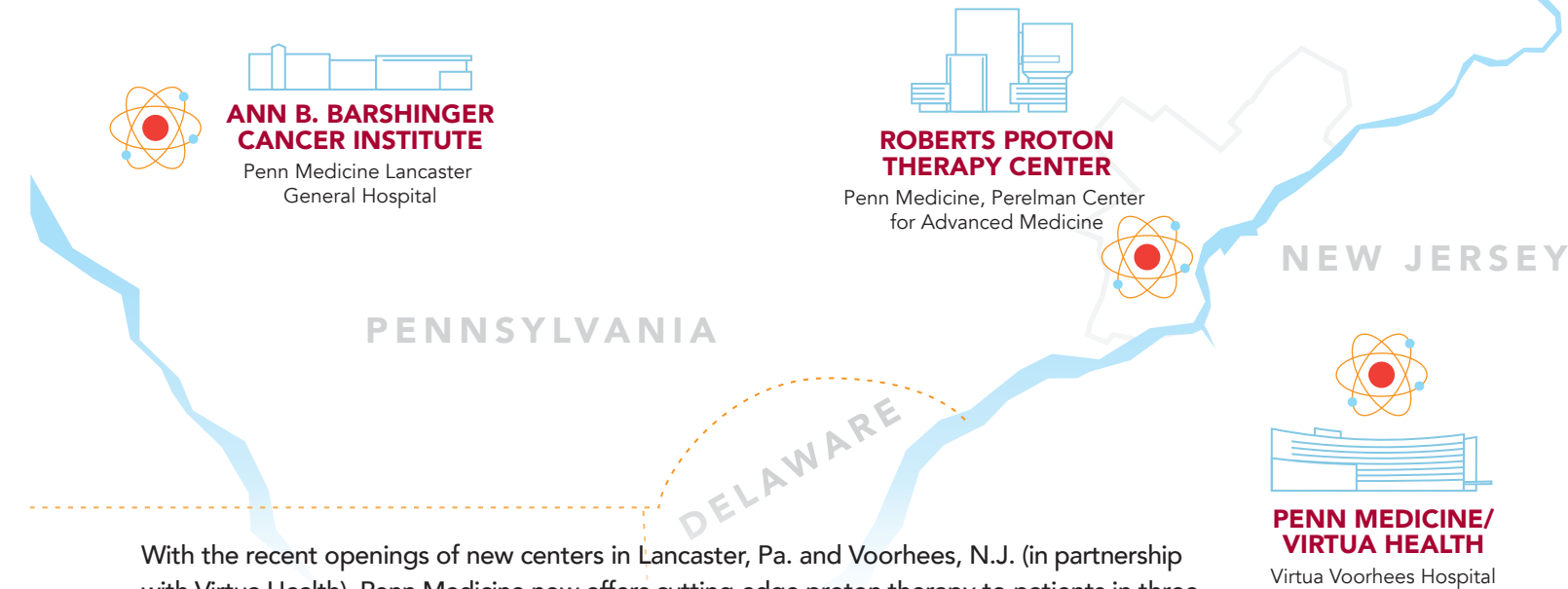
Serving on a steering committee for a statewide initiative to encourage hospitals to do equity work in Pennsylvania, Aysola recently helped define incentives for steps like tracking demographic and social needs data, and forming a community advisory board to help guide performance improvement goals.

"What we showed at Penn was that there are building blocks that have to first be in place for health systems to effectively identify gaps and then address them," she said. "If you jump ahead and only incentivize the end goal [such as preventing hospital admissions], you may not achieve it."

As a result of the new initiative, Penn Medicine, along with many health systems across the state, received millions in incentive awards for such equity work, with more to come.

▶ [Read more about CHEA's work and influence on state policy at PennMedicine.org/news/news-blog.](https://www.pennmedicine.org/news/news-blog)

NEW OPTIONS FOR PROTON THERAPY



With the recent openings of new centers in Lancaster, Pa. and Voorhees, N.J. (in partnership with Virtua Health), Penn Medicine now offers cutting-edge proton therapy to patients in three locations across the metro Philadelphia region. Through research, Penn is defining the best uses of the technology. The new centers ensure that patients outside of Philadelphia can access proton therapy without needing to travel to the city, potentially saving hundreds to thousands of hours of travel time over the course of treatment.

ANYONE CAN RING, FOR ANY REASON

The Abramson Cancer Center reimagines the role of the cancer bell.

Getting to "ring the bell" has been a longstanding tradition for cancer patients celebrating the end of treatment. It has always been a joyous occasion, but in recent years, staff with the Abramson Cancer Center (ACC) at Penn Medicine began to realize that not everyone felt like celebrating when they heard the sound of the brass bell.

"It started to feel controversial when we took a look at all the patients getting maintenance therapy that would not have the opportunity to ring the bell, or other patients who had previously rung the bell, then had their cancer return and now had to hear the bell ringing, which could potentially bring back those sad memories," said Lindsey Zinck, RN, MSN, OCN, chief nursing officer of the cancer service line at the ACC.

That's why, in the last few years, the staff at ACC's locations has been working to make bell-ringing more inclusive. Now, patients can ring the bell at the end or beginning of their treatment cycle; for any type of good news, like an improved CT scan; or for when they aren't feeling good and need to rally. The staff may also choose to ring the bell for personal or professional milestones. No longer is the bell ringing only for certain people. It's for everyone.

▶ [Read more at PennMedicine.org/news/news-blog.](https://www.pennmedicine.org/news/news-blog)



THE NEXT CHAPTER

For Alison Loren, MD, thinking broadly and inclusively is key to her new leadership of the Hematology/Oncology division at Penn.

The division of Hematology and Oncology is one of several in the Perelman School of Medicine's department of Medicine with a name that joins two or more distinct specialties together with an "and." But as indicated in its name, more commonly expressed with only a slash, as Hematology/Oncology, this division has a culture of bringing people and ideas closer together. Many top-tier academic institutions separate these specialties, or they focus on oncology within the context of a stand-alone cancer center, with hematology at arm's length. But at Penn, those who study and care for blood diseases like hemophilia work shoulder-to-shoulder with physicians caring for patients with colon, lung, or other so-called "solid" tumors, as well as with sub-specialists who care for blood cancers and perform cellular therapy and bone marrow transplants.

Alison Loren, MD, who became chief of Hematology/Oncology in September 2022, refers to it as a "liberal-arts division" partly for that reason — but she's quick to note that, while she embraces the term, it isn't one of her invention. Loren stepped into this role in the 50th anniversary year of

the division, as only its fifth chief, most recently succeeding Lynn M. Schuchter, MD, the Madlyn and Leonard Abramson Professor of Clinical Oncology, who served to great acclaim for 15 years. The division, together with the Abramson Cancer Center, which celebrates its own 50th birthday this year, has a storied past.

David Vaughn, MD, a professor and vice chief for clinical affairs in the division, has chronicled its history and growth from a small cadre of hematologists and, initially, one medical oncologist, to a powerhouse division changing the face of medicine. For a book published last year, *Discovery and Healing: Reflections on Five Decades of Hematology/Oncology at the Perelman School of Medicine at the University of Pennsylvania*, Vaughn interviewed all of the living past division chiefs, as well as dozens more faculty who, together with important philanthropic contributions, drove the division forward.

Recently, he sat down to interview Loren, his longtime colleague and new chief, to discuss her plans for the next chapter of that history.

David Vaughn: What have you learned from the division's past chiefs that you now bring into your role?

Alison Loren: The nature of academic medicine has really changed over that 50-year timeframe. There are lessons that you can draw from each of those people but adapt them to today's culture. I didn't know Dr. [Richard "Buz"] Cooper, although I know he was a giant. Dr. [Sanford] Shattil showed a great passion for intellectual achievement.

Steve [Emerson, MD, PhD] is a Renaissance man and he knows something about everything. He impressed on me how important it is to be broad in your thinking and appreciate the nature of our "liberal arts" hematology/oncology program. You should think about arts and humanities and not just about the science, and you should think about the whole patient and what you can bring in from other disciplines to enhance what we're doing.

Following in Lynn's footsteps now is humbling. Not only is Lynn a strong leader, an accomplished scientist, and a wonderful doctor, but she also radiated a feeling of warmth, that this was her family. What I learned the most from her is her inclusivity and belief in a big tent. She includes staff and the teams from our satellite sites. And she treats everyone equally. I hope to continue in that tradition.

What are the benefits of having a division of Hematology/Oncology, as we have at Penn, compared to other institutions where medical oncology and hematologic malignancy, and classical hematology, are separate divisions?

It keeps us all very humble and appreciative of what we don't know and how many wonderful experts we can tap as colleagues. And it's a good way to think more globally about how to advance the whole mission.

A lot of our peer institutions are cancer centers. They're very focused on cancer care only, which can be great, but sometimes means that you're not thinking about all the other things that might happen to a patient or other areas of expertise they need.

A great example is gene therapy for the hemoglobin-related disorders thalassemia and sickle cell. We are experts in gene therapy and cell therapy at Penn Medicine. We do it all the time for our cancer patients now. One of our colleagues, Dr. Farzana Sayani, established the first adult thalassemia program in the country, and it is still one of only two. She also directs the Penn Comprehensive Sickle Cell Program. Kids who are born with these serious blood disorders are largely cared for at pediatric centers, like Children's



David Vaughn, MD and Alison Loren, MD

Hospital of Philadelphia (CHOP). We now have a fairly large population of thalassemia patients who are adults, who are aging out of CHOP. Now there are newly approved cellular gene therapies for these blood disorders. As a leader in creating and treating cancer patients with cellular and gene therapies, we are ready for that. We're going to be the first adult thalassemia gene therapy program to open in the country because we know how to do this.

How do you plan to promote the values of diversity, equity, and inclusion within the division?

The most important thing is having fellows and physicians and staff and nurses and advanced practice providers (APPs) who represent the diversity of our community. And I'll be honest, we are a ways from that, particularly for physicians from backgrounds underrepresented in medicine (UIM). Nationally, the percentage of UIM racial and ethnic minorities in hematology/oncology is lower even than other specialties. Our division's efforts to improve diversity are led by our vice chief for DEI, Dr. Yehoda Martei. Under her leadership, we have implemented several programs to introduce high school, college, and medical students from under-represented backgrounds to our specialty. We hope that by enriching the pipeline of trainees with diverse backgrounds, we will ultimately see better representation among our faculty ranks.

Focusing on our care for marginalized patients in need is really important, too. Within classical hematology, especially, sickle cell anemia is a devastating health issue that is especially common among Black patients. We know that patients with sickle cell disease do better when they are

cared for in a comprehensive sickle cell center. There are several FDA-approved drugs to reduce complications in sickle cell, and we know statistically that there are more patients with sickle cell disease in Philadelphia than are being cared for in a comprehensive sickle cell center. And so we are working on our community outreach, trying to build trust in that community.

What's your vision for the future of the division? Where do you see us 10 years from now?

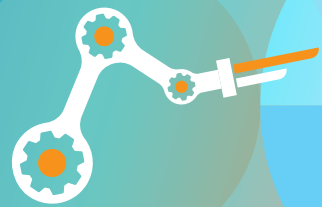
I believe we'll be even awesomer than we are now — we're us, but better. I envision a place where everyone is excited to come to work. We can offer the very best patient care — we are continuing to pioneer the newest advances in genetic, targeted, immune, or cellular therapy. We are actually giving these cutting-edge therapies to patients in our clinics and hospitals every day. We have all the right supports in place to provide care to every aspect of our patients and their lives — supporting them in all the right ways. We have the right staff and the right resources to provide the right care at the right time in the right place, in the best possible way. We are already doing so much of this, but we will do it even better ten years from now. We will keep recruiting the best trainees, supporting the outstanding research that's already flowing on a smooth path, being willing to take risks and make investments to move the field — and our division — forward. When I'm ready to step down, that's how I'd like to leave things.

► [Read an extended version of the conversation online at PennMedicine.org/magazine.](https://www.pennmedicine.org/magazine)

MAKING WHAT'S NEXT IN MEDICINE

By Karen L. Brooks

Since 2017, the FDA has approved more than two dozen new therapies with roots at Penn Medicine — almost half of which are first-in-class for their indications. Becoming a hub for drug research and development took a lot more than luck.



The news reached Abramson Cancer Center (ACC) Director Robert Vonderheide, MD, DPhil, at 11 a.m. on August 30, 2017: The U.S. Food and Drug Administration had officially approved a Penn Medicine-developed personalized cellular immune therapy.

Six hours later, Vonderheide was standing atop a coffee counter in the atrium of the Perelman Center for Advanced Medicine, addressing hundreds of jubilant faculty and staff members who had gathered for a now-iconic “flash mob” celebration of the milestone. Carl June, MD, and a team of scientists, physicians, and other dedicated staff had together turned a dream of using patients’ own immune cells to treat their cancer, into a reality.

Vonderheide called the discovery “a 20-year overnight sensation.” It would be a defining moment for Penn’s identity as a place that incubates and brings to life some of the most transformative advances in modern medicine.

The approval of chimeric antigen receptor (CAR) T cell therapy didn’t happen at Penn Medicine by chance. Nor did the others that followed. Since that day, other research that had been underway at Penn Medicine directly influenced at least two dozen more approvals granted to drugs and medical technologies — giving the stamp of safety and effectiveness needed for these treatments to be widely available to patients outside of clinical trials. Eleven of the advances documented to date represent the first in their classes: eight under cancer, two under gene therapy, and the revolutionary mRNA technology that powers COVID-19 vaccines around the world.

Penn Medicine faculty may lead this crucial work at different points across the continuum of discovery, from conducting pivotal discovery science in the lab which leads to licensing of compounds and technologies by commercial partners, to leading clinical trials of new therapies initially developed outside of Penn.

The list of Penn-linked approvals is growing with each passing year, and for good reason. Science has shifted toward more discoveries based on the underlying mechanism of disease, especially in cancer. Through a particularly robust clinical trial and commercialization infrastructure, Penn has further worked to smooth every part of the path from idea to implementation. And to ensure that state-of-the-art treatments reach the patients who need them, Penn Medicine teams have also kept focus on equity and access during clinical trials and after therapies are approved.

In the long view, Penn’s emergence as a hub for drug research and development is a credit to both the culture and

strategic choices going back decades, says Jon Epstein, MD, executive vice dean and chief scientific officer in the Perelman School of Medicine.

“Our leadership has been judicious about investing in a broad portfolio across a pipeline of development that might take 20 or 30 years,” Epstein says. “People here embrace a no-risk, no-reward approach — they aren’t afraid to take the long view and realize you have to back many different ideas to end up with just a few breakthrough therapies.”

Barrier Free

Hiring Carl June — whose belief that the immune system could be trained to fight cancer was derided by naysayers — in 1999 is one of the risks Epstein references. At the time, nobody predicted June’s work would change the entire trajectory of cancer care.

June began studying CAR T cell therapy in cancer in the late 1990s, and as signs of success grew, so did the breadth of collaborators at Penn Medicine and Children’s Hospital of Philadelphia (CHOP) who brought the method into clinical trials. It would take nearly two decades to achieve FDA approval of the therapy in 2017 as a treatment for advanced acute lymphoblastic leukemia. The groundbreaking technique involves taking T cells — part of the immune system — from a patient’s blood and engineering them to produce CARs before reinfusing them into the body. These new receptors latch onto unique antigens on the patient’s tumor cells, killing them. Marketed by Novartis as Kymriah, the first CAR T cell therapy has proved lifesaving for many patients whose cancer has relapsed or failed to respond to other therapies. It has since garnered two additional approvals from the FDA to treat other forms of cancer.

Similar stories have played out on campus over and over. Jean Bennett, MD, PhD, and Albert Maguire, MD, were also “risky” hires whose ambitions vexed skeptics when they joined Penn’s Scheie Eye Institute in 1992. But their determination and decades of work from basic science through to clinical trials at Penn and CHOP, paid off; in December 2017, less than four months after approving CAR T, the FDA approved the married team’s treatment for a rare form of congenital blindness called Leber congenital amaurosis. Marketed as Luxturna, the therapy restores patients’ eyesight by injecting a corrective gene directly into their eyes via a viral vector. It was the nation’s first commercialized gene therapy — a term that encompasses a collection of techniques to modify a patient’s DNA — for a genetic disease.

them. But at Penn Medicine we integrate our clinical and research missions intentionally, for the sake of the patients who don't have the best clinical options today. We can't afford not to invest back into ongoing scientific discovery."

Next Generations

The FDA's approval of a drug doesn't mean its development ends, particularly in young and still-unfolding categories like cell and gene therapy and mRNA technology. Research around the world has proliferated in these new realms, where Penn Medicine faculty are still striving to push the science forward.

While CAR T cell therapy has revolutionized treatment for hematologic malignancies, researchers are still striving to use it successfully against solid tumors; getting the treatment to penetrate solid masses is one challenge, and it is harder to find unique antigen proteins to target on solid tumor cells. Faculty members are examining ways to overcome these limitations, such as delivering CAR T cells regionally and testing multivalent CARs, which simultaneously bind to multiple targets.

Researchers are also pursuing universal "off-the-shelf" versions of CAR T, which would spare patients from having to donate their own T cells for engineering — saving precious time while ensuring an abundance of high-quality cells to work with. And many are studying CAR T therapy in conditions other than cancer — including Epstein, who is evaluating CAR T cells' ability to treat fibrosis, which can affect any organ and is a major driver of heart failure.

In terms of gene therapy, most activity to date has tackled rare diseases, but some faculty are on a mission to change that — like cardiologist Kiran Musunuru, MD, PhD, MPH, ML, director of the Genetic and Epigenetic Origins of Disease Program. Musunuru is applying the gene editing technology CRISPR to fight the leading cause of death worldwide: cardiovascular disease. He has found that modifying genes in the liver can permanently reduce a person's cholesterol levels and protect against heart attack and stroke. Currently in a clinical trial in New Zealand and the U.K., this single shot could eventually work as a heart disease "vaccine."

And when it comes to mRNA, "we're working on every imaginable infectious disease," says Weissman, who back in 2005, alongside Karikó, discovered how to modify mRNA so it could be used safely and effectively in vaccines and

therapeutics. Even before COVID-19 struck, Weissman's lab group had set up mRNA vaccine clinical trials for herpes, HIV, and influenza. The many avenues they are currently exploring include a universal flu vaccine that covers all 20 known subtypes of influenza virus and an all-in-one "pan-coronavirus" vaccine that would be effective against any new variants yet to emerge.

People suffering with a broad range of life-threatening illnesses today hold onto hope that tomorrow will bring a new therapy that will save their life. Across Penn Medicine, researchers are focused on developing new medicines to address their unmet needs.

"With Penn at the forefront, the application of these first-in-class therapies to a broader array of other diseases is just around the corner. Penn Medicine's scientific impact — and the worldwide attention it commands — have never been greater," says J. Larry Jameson, MD, PhD, executive vice president of the University of Pennsylvania for the Health System and dean of the Perelman School of Medicine. "It is a tremendous point of pride that innovation born within our laboratories is being deployed to save lives across the world, and we are committed to fostering breakthroughs that will continue to redefine medicine as the 21st century unfolds."

Eighteen months later, approval followed for Zolgensma, a gene therapy using a viral vector developed in the lab of James Wilson, MD, PhD, director of Penn's Gene Therapy Program and Orphan Disease Center, and studied in trials at CHOP, to correct spinal muscular atrophy — the number one genetic cause of infant mortality.

And in the most ubiquitous novel advance tied to Penn Medicine, in August 2021 the FDA gave its first full approval to an mRNA-based COVID-19 vaccine, which uses technology discovered more than 15 years earlier by longtime research partners Drew Weissman, MD, PhD, the Roberts Family Professor in Vaccine Research, and Katalin Karikó, PhD, an adjunct professor of Neurosurgery.

Recruiting faculty who dream big is essential to drug development, but there are other reasons Penn Medicine has connections to so many cutting-edge therapies. Among the top, says Vonderheide, is a strategic emphasis on translational research and eliminating barriers between laboratories and the clinic.

"Even our building design reflects that value. If you stand in the lobby of the Perelman Center for Advanced Medicine, you're within 100 yards of the labs where discoveries are being made, the clinics where clinicians are designing clinical trials and patients are getting therapies, and the offices where executives are working out financial models," he says. "We're a unified, integrated system committed to making science real for patients."

Financial investment from the health system is key to moving discoveries toward the clinic and helping more patients, Epstein adds, citing the Perelman School of Medicine's Clinical Cell and Vaccine Production Facility — where cell and gene biotherapeutics are manufactured to meet regulatory standards — as an example.

"The health system invested in what was only basic research at the time to build the good manufacturing practices facility that is necessary to produce things like CAR T cells safely so they can be put back into humans," he says. "Facilities like that cost a lot, and most medical schools can't afford



Drew Weissman, MD, PhD, and Katalin Karikó, PhD, made fundamental discoveries that made it possible to use mRNA for vaccines and therapies — a technique used to develop two of the first approved COVID-19 vaccines.

THE PATH FROM INNOVATION TO IMPLEMENTATION

Penn's infrastructure in both supporting clinical research and forging commercial partnerships smooths the way from idea to approval.

In the sea of smiling faces at the August 2017 CAR T flash mob celebration, John Swartley, MBA, PhD, was beaming as much as everyone else — but not just because of Kymriah's approval. His grin was sparked by memories of one of the first meetings he had at Penn, right after joining the institution in 2007.

The meeting was with a “very frustrated” Carl June.

“Carl was struggling to find funding for this phase one study — the study that eventually became the *New England Journal of Medicine* article that kicked off the whole CAR T revolution,” Swartley remembers. “Fifteen to 20 years ago, you really could not raise money for cell and gene therapy. But he knew the world was going to wake up to it, and part of my job was to believe him before everyone else did.”

Swartley was hired into Penn's Center for Technology Transfer (CTT), a “more or less traditional, transactional tech transfer group” that managed the patenting and licensing processes for any intellectual property developed university-wide. Gradually, he helped transform it into the Penn Center for Innovation (PCI), which still serves those functions but is now equally focused on building relationships between faculty innovators and the private sector.

“Faculty know to disclose big discoveries to us, but also to come to us if they're looking for sponsored research or thinking that maybe they should start their own company — whatever's the best way to take their program forward and get it to patients,” says Swartley, who today is associate vice provost for research at Penn and PCI's managing director. “PCI comes in at the earliest stages of these discussions and also brings opportunities to faculty without being asked. We're the matchmaker, the intermediary — the enzyme that helps make a reaction happen. But we're not consumed in the reaction, so then we go off and find another partnership to build.”

The Slow Motion of Drug Development

These days, PCI handles around 750 commercial agreements annually, about three-quarters of which involve Penn Medicine. Such agreements can prime early discoveries like new medicines for success years — sometimes decades — before the words “FDA approval” are ever uttered.

Drug development generally moves at a snail's pace, with therapies taking an average of 10 to 15 years and costing upwards of \$1 billion to trudge from concept to market. For every drug that “makes it,” more than 5,000 fail.

Anyone working in academic medical research is aware of the long and winding pathway an experimental therapy must traverse before securing approval. Often, the journey begins once a disease mechanism is identified, and then the search for a target molecule to fix it begins in the laboratory. Testing begins in cells outside the body before progressing in animal models. A small-scale phase 1 clinical trial then examines a compound's safety in humans, followed by a phase 2 trial that measures its effectiveness and a large-scale phase 3 trial studying it in various populations, dosages, and combinations with other drugs.

While PCI manages all of the intellectual property coming out of Penn as a whole, Penn Medicine has its own discrete resources for supporting faculty research efforts as they push new therapies through the pipeline. The dozen staff members on the PSOM Office of Clinical Research's (OCR) regulatory team, all of whom have regulatory backgrounds and graduate degrees in biomedical science, guide researchers in designing their projects with a view toward FDA approval — offering know-how that doesn't exist in most academic organizations, according to Emma Meagher, MD, senior vice dean for clinical and translational research, who oversees PSOM's clinical research infrastructure.

That regulatory expertise is a layer on top of the support that clinical research offices routinely provide academic health centers for the essential elements of simply running a clinical trial, which is not simple at all. Services range from participant recruitment and staff training to financial planning to legal guidance through compliance and contracting for



Carl June, MD, spoke before the flash mob that gathered in August 2017 to celebrate the approval of the first CAR T cellular therapy.

corporate-sponsored trials. By streamlining all of the processes involved in clinical research, Penn's OCR empowers faculty to conduct higher-impact trials that boost clinical discovery and offer patients more advanced treatment options and opportunities.

"As academics, we write grants, we publish papers, we execute research — but we don't necessarily do that through the lens of, 'How would this actually get reduced into clinical practice? What are the requirements I need to demonstrate to get there? How would this be manufactured, and what would scale-up look like?'" Meagher says. "There has been an enormous investment in taking Penn's scientific heft and enabling its translation toward product development by hiring people who have a deep understanding of how regulatory authorities consider new drugs and devices."

Partners in the Path to Approval

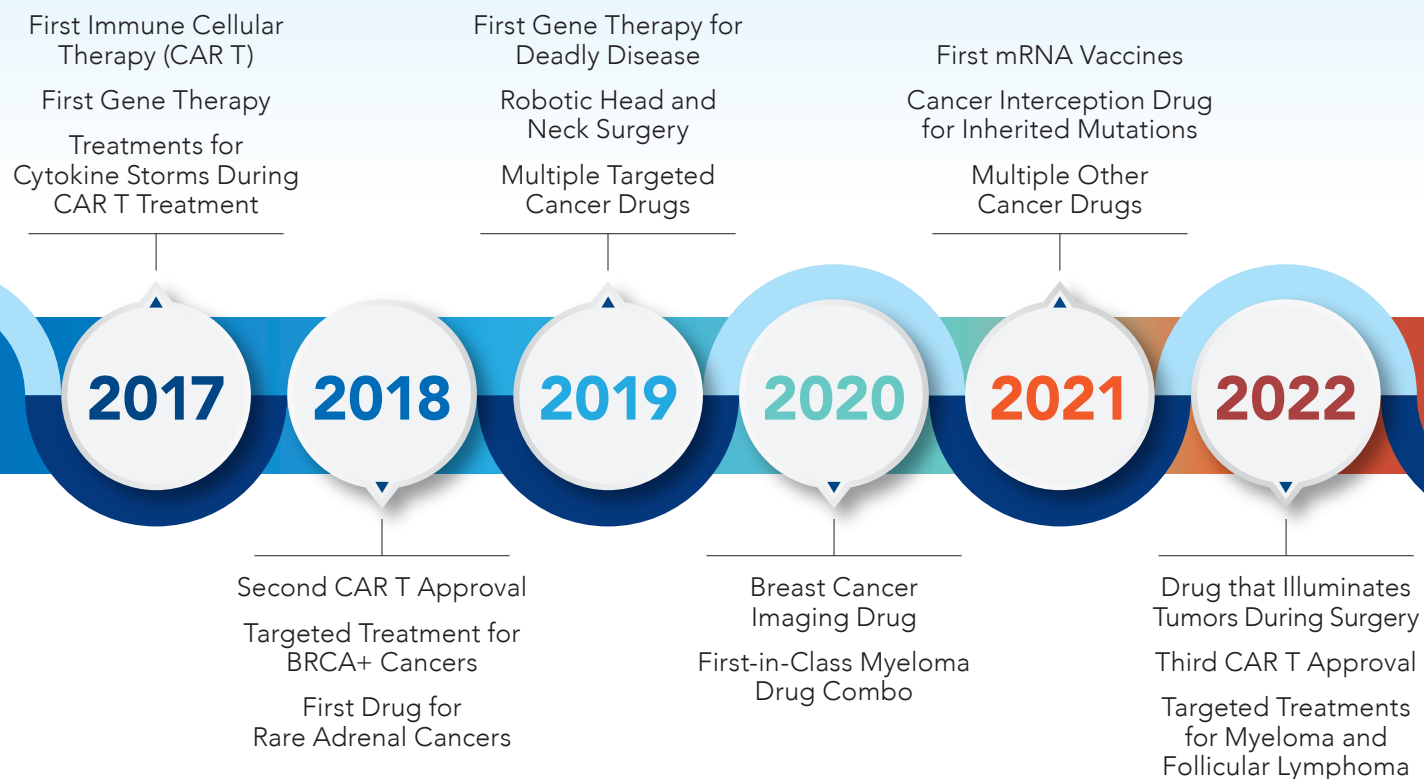
The expansion of PCI — now about three times the size of its predecessor, the CTT — has empowered researchers to accelerate the advancement of their discoveries by positioning them as active research and development partners with pharmaceutical and biotech companies.

"We're no longer just a contracting entity whose work ends with throwing a discovery over the fence. We're officially joint developers of our own technologies, especially when it's something like a groundbreaking cell or gene therapy, because without our faculty members' skills and expertise, these types of transformative innovations don't work," Swartley explains. "Penn helps its faculty embrace roles as collaborative co-development equals rather than waiting for an outside company to swoop in and take over."

In many cases, PCI's role is to support faculty in founding their own startups. Successful Penn Medicine spinout com-

TRANSLATING **DISCOVERY** INTO **MEDICINE**

Year after year, more therapies rooted at Penn gain approval by the Food and Drug Administration.



A comprehensive list of FDA approvals from the last decade based on Penn research is currently under development. To see a list and description of cancer-related approvals documented since 2017, visit [PennMedicine.org/magazine](https://www.pennmedicine.org/magazine).



panies developing cellular therapies such as Tmunity (now a division of Kite, a Gilead Company), Carisma Therapeutics, and Capstan Therapeutics, are all excellent examples of this, Swartley points out. Further developing promising technologies through a startup can be a wiser strategy for commercializing the technology than immediately licensing it to an existing company, he says, because startups (and the types of firms that invest in them) are often more comfortable with the myriad risks inherent in early-stage product development. And because startup companies need early financial investment to grow, since 2018, Penn Medicine has supported a growing number of these faculty-led spinoff companies through the Penn Medicine Co-Investment Program. As of the end of the 2022 fiscal year, the program had invested over \$35.5 million in nine Penn Medicine spinouts that have gone on to cumulatively raise over \$1.4 billion in capital.

As a basic scientist himself, Jon Epstein remembers that early in his career, he routinely imagined "somebody else — probably a pharmaceutical company — taking my discovery and running with it."

"I thought someday they'd read a paper I'd written and go make a new medicine," Epstein recalls. "But being at Penn has changed me. Now, I think I could make a new therapy here."

No matter how far down the testing and development pathway an investigator's project perseveres, Meagher says it demands doggedness and drive to navigate the laboratory, clinical, and entrepreneurial routes involved in drug discovery: "It takes a combination of incredible passion for and curiosity in the science, an unbelievable sense of optimism, and being able to take the knocks — to have an inherent resilience to bounce back up again even if nothing is ever going to go the way you want it to go."

Except sometimes, eventually, things do go the way a researcher wants — like they did for June. Two years after first lamenting to Swartley about his lack of funding, June secured just enough private funding to treat three patients in an initial trial. Then, in 2012, two years after those remarkable first results were published — with support from Swartley and his team — Penn signed an agreement with Novartis to accelerate research, development, and commercialization of CAR therapies.

Five years after that, their voices joined the chorus of cheers at the CAR T approval flash mob event.

And the rest is history that is still making history.

FROM SERENDIPITY TO SCIENCE-DRIVEN DRUG DESIGN

The approval of CAR T cell therapy ushered in a new era for cancer treatment.

In the five years since the FDA's initial approval of CAR T cell therapy, Penn Medicine has gleaned 20 additional approvals related to drugs and techniques to treat or detect cancer.

Rather than being the single disease class many people refer to, "cancer" is a blanket term that covers more than 100 distinct diseases, many of which have little in common aside from originating with rapidly dividing cells. Since different cancers demand different treatments, it follows that a large number of new therapies emerging from any institution would fall under the oncology umbrella.

But why so many in just this five-year period?

The volume makes sense, says ACC Director Robert Vonderheide, attributing the flurry to a recent "explosion" in knowledge about cancer biology.

"Much of that knowledge is about the immune system's ability to attack cancer, which people seriously doubted until about 20 years ago. As soon as we had a clinical validation for this Achilles heel in cancer, the dam burst for ideas about other ways to exploit that vulnerability to come forward," he says. "The first drug that came out to activate the immune system inspired the rest of the field to find the next drug, and the one after that. We as a field have moved from serendipity and empiricism to science-driven drug design."

The first CAR T cell therapy approval invigorated faculty interested in finding new ways to harness the immune system to fight cancer.

"An approval like that makes what you're working on more of a reality," says Avery Posey, PhD, an assistant professor of Systems Pharmacology and Translational Therapeutics whose lab team spends much of its time trying to identify more specific antigens for solid tumors and also studies ways to optimize engineered donor T cells. "It brings a new perspective, showing that your work is more than basic research and can actually become drugs that impact patients' lives. That's a real motivator to keep pushing forward."

Honing new immunotherapies is a priority among Penn researchers, but not all of the recently approved cancer-care tools developed at the institution engage the immune system. Faculty have explored and introduced widely varying approaches to improving the standard of care for cancer patients.

For example, there's olaparib (marketed as Lynparza), which is used in ovarian and breast cancers, most commonly those involving an inherited BRCA gene mutation. The oral medication works by targeting PARP, an enzyme in the body that helps to repair damaged cells — including cancer cells. By inhibiting PARP, the drug stops the repair of cancerous cells to prevent them from growing. The drug's approvals in 2014, 2018, and 2022 were based on trials led or co-led by Susan Domchek, MD, executive director of the Bassett Center for BRCA at the ACC.

There's also pafolacianine (marketed as Cytalux), the first FDA-approved agent that illuminates ovarian cancer and lung cancer lesions during surgery, enabling surgeons to find and remove cancerous tissue. Penn investigators Janos Tanyi, MD, PhD, and Sunil Singhal, MD, led its Phase 2 and 3 clinical trials leading to approval. And belzutifan (marketed as Welirig), the first treatment of its kind for treating von Hippel-Lindau disease-associated tumors, such as those in renal cell carcinoma and central nervous system hemangioblastomas — a drug with Penn connections from basic science discovery about cancer hypoxia through to the definitive clinical trial leading to its approval.

On Jan. 12, 2023, the American Cancer Society released its annual compilation of cancer facts and trends, which reported



Sunil Singhal, MD (right), led trials of pafolacianine, an agent that lights up lung cancer tumors to help surgeons find and remove cancerous tissue. Photo credit: Addison Geary.

that since its peak in 1991, cancer mortality in the U.S. has dropped 33 percent.

"That's almost 4 million deaths averted. Clearly, something dramatic has changed the outlook for patients with cancer in this country in the last 30 years," Vonderheide says.

"Much of that has to do with new therapies, which were all unknown drugs in a phase one clinical trial at some point. Every single drug you see advertised on TV — once upon a time, some patient somewhere was the first patient ever treated with it. This is why we do what we do."

Because of high mortality outcomes among cancer patients who haven't responded to conventional therapies, risk tolerance in cancer clinical trials tends to be higher than in trials testing novel therapies for non-cancer conditions, Emma Meagher explains

"High-risk, and potentially high-reward, trials happen frequently in cancer for that reason and oftentimes can move more quickly," Meagher says.

Just because a new drug is first tested and approved to treat cancer doesn't mean it can only treat cancer, though. Many therapies that start in oncology eventually have broader disease applications — like CAR T cell therapy, which is already showing promise with other diagnoses, like the autoimmune disease lupus.

CAR T cell therapy's potential translation to other diseases is "a rumble that is beginning to sound like thunder in autoimmune disorders, neurological conditions, rheumatological conditions, and dermatological conditions, among others where immune mechanisms are implicated," she adds. "We're beginning to see momentum in using what is currently considered a cancer therapy well outside of the oncology space, and I predict that Penn will be a real leader in this area."

PUTTING ADVANCES WITHIN REACH

Treatments and vaccines are only useful in the hands of people who need them.

Despite Penn's track record developing therapies that make it onto the market, faculty remain humbled by one basic tenet: Advances mean nothing if patients can't access them.

"If our goal is to improve human health, we cannot call ourselves successful unless we bring the fruits of our labor to bear as broadly as possible on people suffering from the conditions that interventions are designed to treat," Meagher says.

In the U.S., manufacturers are free to set prices for brand-name drugs and launch novel products at the highest rates, with gene therapies often costing millions and CAR T treatments approaching the half-million-dollar range. Although some manufacturers offer payment assistance programs, these expenses burden state and federal health programs, private insurers, and uninsured or under-insured patients facing out-of-pocket costs.

Commercialized drug prices are beyond an academic institution's control, but researchers — including many at Penn — are exploring advances that would make cutting-edge treatments more easily available to everyone who needs them. In the case of CAR T, for example, those working to develop a universal version of the therapy understand they can drive down costs by transforming a time-intensive, personalized treatment that requires a patient to donate

their own T cells into one where an existing bank of cells could be used to treat many patients.

Many U.S. cancer patients who are eligible for today's FDA-approved CAR T therapies do not actually receive the treatment or end up waiting months to begin the process as their disease worsens. Honing an "off-the-shelf" version of CAR T therapy would also curb the extensive wait times and manufacturing limitations that prevent many patients from getting the treatment.

Clinical Trial Outreach

Racial and ethnic health disparities also stoke accessibility concerns. Black Americans are less likely than any other group to receive CAR T cell therapy — a trend rooted in gaps in income, education, housing, job security, and proximity to high-quality medical centers. These same social determinants of health have also led to their underrepresentation in CAR T and all kinds of clinical trials; Black patients account for just 5 percent of clinical trial participants nationwide.

"Black patients' historically low participation in trials means that, compared to white individuals, they have less

access to some of the most advanced new treatments," says Carmen Guerra, MD, MSCE, vice chair of diversity and inclusion in the Department of Medicine and associate director of diversity and outreach at the ACC.

To better diversify clinical studies, the ACC recently conducted a five-year community engagement study that reached more than 10,000 individuals through marketing campaigns tailored to minority cultures; wellness forums and events in Black communities; partnerships with Lyft and Ride Health to reduce transportation barriers; and patient education efforts. By the end of the project, the number of Black patients in Penn's cancer clinical trials had doubled.

Additionally, the ACC piloted a Cancer Clinical Trials Community Ambassador Program that trained Black cancer survivors and caregivers in how to inform their networks about the importance of clinical research; a Genentech Innovation Grant launched in February is now fueling a study to determine how effective these peer ambassadors are when matched with newly diagnosed or relapsed breast cancer patients. And a first-of-its-kind collaboration with the Lazarex Cancer Foundation allows Penn to reimburse trial participants for gas, parking, plane or bus tickets, hotels, and other out-of-pocket travel and lodging costs related to clinical trial participation for the patient and a companion.

"There is financial toxicity associated with participating in a clinical trial, even though the actual treatment is covered by research dollars," Guerra says. "We're working to eliminate obstacles one by one to make sure people can get the treatments they need. Addressing inequities is like an onion — we peel off one layer of barriers, then see what's underneath so we can address the next layer."

Global access concerns abound, as well. Outside the U.S. and other economically stable nations like China, Australia, Singapore, and the United Kingdom, CAR T cell therapy is unavailable. Penn Medicine and CHOP have begun to partner with low- and middle-income nations in an attempt to facilitate global equity in CAR T cell research and treatment. Their first agreement is with Costa Rica's Social Security Program, the Caja Costarricense de Seguro Social; the partners will bring adult and pediatric patients to Penn or CHOP, where their immune cells will be collected for manufacturing into CAR T cells. Then, those cells will be returned to Costa Rica for infusion as part of a trial to be conducted there.

Democratizing Vaccine Access

Even when drugs are relatively affordable and easy to produce, racial disparities persist — disparities Penn Medicine is striving to overcome. Following the approval of mRNA vaccines against COVID-19, for instance, the health system worked with partners in West and Southwest Philadelphia to bring vaccines directly to their predominantly Black communities in spaces like gyms and public schools, and later moved portable

"hyperlocal" clinics between locations like fast-food restaurants and retail parking lots in neighborhoods where many residents remained unvaccinated.

And like with CAR T, the global distribution of mRNA vaccines is far from equitable. By the end of 2022, at least three-quarters of the population in dozens of countries had been fully vaccinated — but in many others, mostly in Africa, only small fractions had received vaccines. More than three years after COVID-19 first emerged, close to one-third of the global population has not yet had a single dose. That's a big problem, says Weissman, who has collaborated on research and drug development with more than 200 academic and biotech labs "on every continent except Antarctica" and has helped foreign governments set up Good Manufacturing Practices (GMP) sites where scientists in underserved areas are trained to produce and administer vaccines. Working with investigators at the vaccine center at Chulalongkorn University in Bangkok, he established a quality manufacturing center to produce an mRNA COVID-19 vaccine for Thailand and seven surrounding low- and middle-income countries, and he has done similar work in Africa and eastern Europe.

"Part of the failure in clearing COVID-19 has been a lack of vaccine access in many regions of the world where unchecked virus replication led to new variants," he explains. "Local groups and governments being able to make their own RNA vaccines is critical for equity. I also believe these GMP sites will offer regions the ability to make vaccines against local diseases that Big Pharma has no interest in, such as dengue and tularemia in Southeast Asia, and malaria and a variety of local pathogens in Africa."

More Work to Be Done

Efforts at Penn to understand gaps in new drug access go as far as examining how and where products end up being prescribed. For example, researchers found in a spring 2022 study of the first-ever mutation-targeted bladder cancer drug that it was being used by fewer than half of patients who tested positive for the gene mutation in question and qualified to take it. Fewer than half of those potentially eligible even underwent testing.

The next step: figuring out why more people aren't accessing a drug that could extend or save their lives and how to help close the gap — in this example, by advocating for more genetic testing and education for treating physicians.

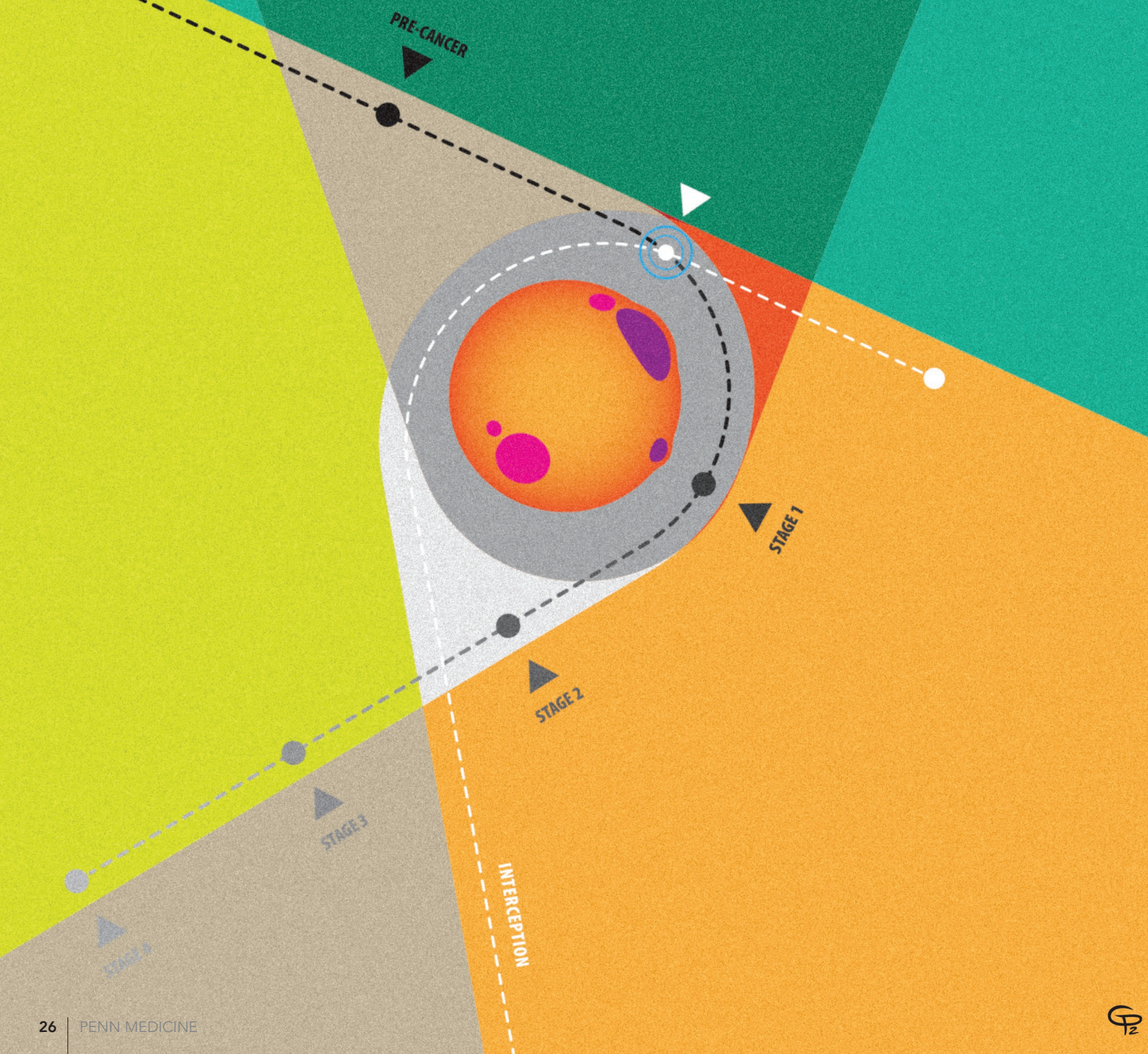
"In academics, our incentive mechanism is to publish, to write grants, to see patients, and to teach," Meagher says. "But if community isn't an integral, systematic part of our processes, we aren't doing our jobs to the best of our ability. If you believe what you're working on is important, you must bring it to all the people it will benefit." □



The New Science of Cancer Interception

By Kirsten Weir

Penn researchers hope to change the game by interrupting the development of more types of cancer at their earliest stages.



Imagine cancer as a line on a chalkboard. At the left is a healthy cell. Reading left to right, you can follow a cell's journey as it begins to develop abnormalities, morphs to become a localized cancer, and finally metastasizes to an advanced cancer at the far side of the spectrum. "As a field, we've been spending a lot of time looking to the right. The opportunity now is to look to the left," says Robert Vonderheide, MD, DPhil, director of the University of Pennsylvania's Abramson Cancer Center and the John H. Glick Abramson Cancer Center Professor in the Perelman School of Medicine. "Can we intercept those precursor lesions before they become cancer?"

That is the promise of the burgeoning field of cancer interception. The goal of interception is to catch, or intercept, cancer cells as they begin to develop into pre-cancers or very early cancers, and halt or reverse that process. The concept isn't unheard of. During colonoscopy, for instance, a gastroenterologist looks for adenomatous polyps that could go on to become colorectal tumors — and snips them out before they can go rogue. That form of mechanical interception saves lives. Now, genetic and molecular tools are opening the door to new methods of interception, for a range of cancer types.

"Interception is not prevention per se, and it's not therapy. It's truly taking the football out of the quarterback's hands," Vonderheide explains. "If we can do this successfully, it will be a whole new space to impact the burden of cancer."

A New Cancer Interception Institute for BRCA

Researchers across Penn Medicine are coming at the study of interception from every angle, including basic science to understand the molecular changes that lead to cancer and to develop new methods for finding it. Much of this work takes advantage of emerging tools, Vonderheide says. New single-cell sequencing technologies, for instance, allow researchers to track changes at the level of an individual cell. Novel mouse models, many developed at Penn, are helping scientists to characterize the changes in pre-malignant tissues. "There's a whole host of technology that is allowing us to find these needles in the haystack," he says.

So far, scientists are largely focusing their efforts on people with a high risk of developing cancer, such as those with genetic variants like *BRCA1* and *BRCA2*. BRCA mutations are well known for their association with hereditary breast and ovarian cancer, and are also associated with prostate and pancreatic cancers. People with inherited BRCA mutations are a natural choice for advancing the science of interception — both because their cancer risk is fairly well quantified, and because they are hungry for better options, says Susan Domchek, MD, executive director of the Basser Center for BRCA at the Abramson Cancer Center and the Basser Professor in Oncology in the Perelman School of Medicine.

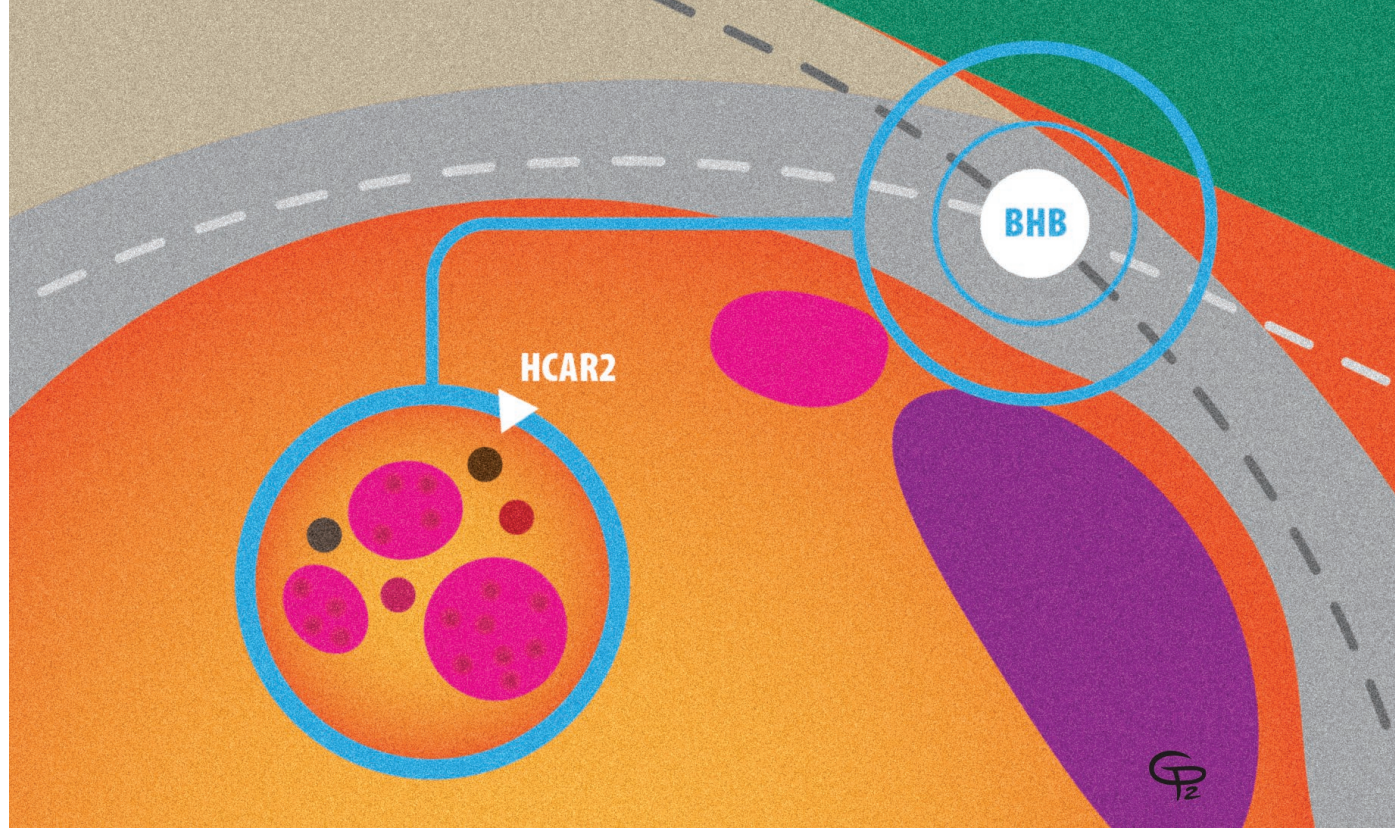
"Interception is not prevention, and it's not therapy. It's truly catching the football out of the quarterback's hands."

— Robert H. Vonderheide, MD, DPhil

"Testing for a BRCA mutation has implications not only for the individual, but for their entire family. It's very personal," Domchek says. "Right now, we tell people they can reduce their risk of cancer by removing the breasts or the ovaries. But we want to offer better options than removing body parts."

The Basser Center was established in 2012 with support from Penn alumni Mindy and Jon Gray in honor of Mindy's sister Faith Basser, who died of BRCA-related ovarian cancer at age 44. The center has been a world leader in BRCA research. Now, Domchek and her colleagues are taking aim at interception. In late 2022, the Grays announced a \$55 million gift to launch the new Cancer Interception Institute at the Basser Center. The Grays' total commitment to Penn over the last decade has now surpassed \$125 million, including their transformative \$25 million gift that established the Basser Center in 2012.

Domchek and her colleagues are launching many initiatives for the new Institute. For example, she is leading a pioneering study testing a new cancer vaccine in women with *BRCA1*



and *BRCA2* mutations. In an initial trial, patients who were in remission after previously having cancer were vaccinated, with the goal of preventing recurrence. Now, she's testing the vaccine in *BRCA*-positive participants who've never had cancer, in hopes that the vaccine response can intercept early lesions before tumors develop. If the approach is successful, it could open the door for intercepting the various cancers associated with *BRCA* mutations.

Other Bassett Center scientists have set their sights on basic research questions that could lead to new avenues to intercept cancer. "Better understanding the molecular biology in which a normal cell becomes a cancer cell is key to understanding the best way to intercept it," Domchek notes. "There's a lot of basic science driving what we're doing, and the purpose of the Institute is to figure out as many of these different possible directions as we can."

One scientist working toward that goal is Katherine Nathanson, MD'93, the Pearl Bassett Professor for *BRCA*-Related Research and deputy director of the Abramson Cancer Center. With support from the Gray Foundation, Nathanson is collaborating with researchers at Harvard University to develop a so-called "human breast atlas." Looking at tissue samples from women with and without *BRCA* mutations, they are mapping the various types of cells present in breast tissue, as well as the molecular changes cells may undergo as they travel left to right along the route from healthy to malignant.

In an initial collaborative study, they've discovered a subset of cells, known as basal-luminal cells, that accumulate with age and appear to display early genetic changes that may be associated with some cancers. Now they're expanding on that work to further determine how factors such as menopausal status or the presence of *BRCA* mutations might influence

those changes. "These are targets for future research," Nathanson says. "We're focusing on high-risk individuals to understand what's happening that may be helpful for preventing disease."

Detecting Cancers Earlier

Realizing the full potential of cancer interception will also rely on advancing the science of early cancer detection — and then continuing to look farther to the left on the metaphorical line on the chalkboard.

That's the goal of an ongoing study by Penn Medicine researchers Erica Carpenter, MBA, PhD'09, director of the Liquid Biopsy Laboratory at the Abramson Cancer Center, and Bryson Katona, MD, PhD, director of the Gastrointestinal Cancer Genetics and Gastrointestinal Cancer Risk Evaluation Programs. They are collaborating to develop new blood-based biomarkers to identify pancreatic cancer at earlier stages. Pancreatic cancer is notorious for going undiagnosed until it is advanced and difficult to treat.

Katona and Carpenter decided to combine multiple biomarkers linked to pancreatic cancer, including circulating tumor DNA, extracellular vesicles and a tumor marker known as CA-19-9. Using machine learning, they developed an algorithm to look for telltale patterns among those multiple markers. "We were able to come up with a blood-based signature of pancreatic cancer that was fairly sensitive and accurate," Carpenter says. "But we felt we could do even better, so we're continuing to refine the test before we test it in the clinic."

Interception in Action

Elsewhere at Penn, interception efforts are already reaching patients. Nathanson, who is developing the pre-cancer atlas for *BRCA* mutations, has also helped to develop an approach to intercept cancer in patients with von Hippel-Lindau (vHL) disease. The inherited disorder causes tumors and cysts throughout the body. Penn patients participated in a trial, led by Vivek Narayan, MD, MSCE'16, an assistant professor of Hematology-Oncology, that led to FDA approval of belzutifan, which inhibits the development of several vHL-associated tumors including renal cell carcinomas and pancreatic neuroendocrine tumors.

Previously, surgery was the only way to treat patients with vHL. Now, they have a new tool to keep tumors at bay. "I have a patient whose mother died from this disease. Now I can treat him in a way we were never able to treat his mother," says Nathanson, who leads the vHL Comprehensive Care Center. "It's a game changer for many of these patients."

Meanwhile, Katona is teaming up with Maayan Levy, PhD, an assistant professor of Microbiology, to study interception in patients with Lynch syndrome. The inherited disorder increases the risk of many cancer types, especially colorectal cancers. Yet even when people have this genetic predisposition, the age of onset and rate of cancer progression varies widely, Levy says. "We now understand that there's a strong environmental contribution to developing colorectal cancer," she adds. "There's an urgent need to understand how we can modify those [environmental] factors to reduce disease."

In a study published in *Nature* in 2022, Levy and her team compared different diets in mouse models of colorectal cancer. They found mice who ate a ketogenic diet, rich in fat but low in carbohydrates, were strikingly resistant to developing colorectal tumors. Investigating further, they zeroed in on beta-hydroxybutyrate (BHB), a molecule produced in the liver in response to ketogenic diets. BHB, they found, suppressed tumors by slowing the proliferation of epithelial cells in the colon. When Levy administered BHB to mice, they developed fewer colorectal tumors — even without the keto diet. What's more, any preexisting tumors appeared to stop growing.

It was an exciting finding, not only because BHB appeared to intercept colorectal cancer so well, but also because the compound is widely available as a diet supplement. Just a few short months after the mouse study was published, Levy and Katona launched a trial supported by the Abramson Cancer Center, still ongoing, to test BHB in people with Lynch syndrome. Participants drink the supplement over four weeks. During routine colonoscopies before and after the intervention, the researchers are collecting intestinal biopsies to see whether the treatment reduces cellular proliferation in the colon.

The four-week course of treatment highlights a unique and important feature of interception: These therapies may not need to be taken long term. Colonoscopy intercepts colon cancer by removing pre-cancerous polyps, effectively resetting the cancer clock. Pharmaceutical interception may work the same way. Vonderheide envisions drugs or vaccines that could be given for a few weeks or months to pick off precancerous cells. Because it takes time for the lesions to regrow, a person might not need a booster dose again for several years. "That decreases drug exposure and minimizes toxicity," he says. "You may be scot-free until it's time to intercept again."

Translational Science at Penn Medicine

Plenty of scientific puzzles remain to be solved before cancer interception becomes the norm. But as the field comes into its own, Penn Medicine is doing its part to answer those questions. The institution has all the pieces to push the field forward, says Levy, who moved her work on intercepting colorectal cancer from mouse models to human participants in a matter of months.

"I think if I worked at a different university, this might have stayed a basic research observation," she says. Fortunately, Katona and his colleagues already had established relationships with Lynch syndrome patients, who come to Penn for regular cancer screenings. "The infrastructure we have here allowed us to move so quickly," Levy adds.

Similar possibilities exist for other hereditary disorders, including patients with *BRCA1* and *BRCA2* mutations. "We have a strong hereditary disease program at Penn, and our ability to link [new therapies] into that program is almost unparalleled. We're amazing at translation," Nathanson says.

At the new Bassett Cancer Interception Institute, and across Penn's labs and clinical spaces, researchers are beginning to realize the potential of interception. "Cancer interception is really a new pillar of cancer treatment," Levy says. "This is not impossible. We have the tools to do it, and we need to be putting in all the effort to make it work." □

► [Read more about cancer interception online at PennMedicine.org/magazine.](https://www.pennmedicine.org/magazine)



THE CROSSROADS

By Christina Hernandez Sherwood

PennHealthX is a student group where future doctors can explore their interests in business and technology. After 10 years, it has surpassed the standard for traditional extracurricular clubs. It has grown, like an entrepreneurial startup in miniature itself, to become an influential student-driven creative hub for projects and programs at the intersection of medicine with other disciplines.

After anatomy lab on a December evening in 2012, first-year medical students Jacqueline Soegaard Ballester and Dan O'Connor helped their classmate Diane Dao to a nearby Starbucks on the University of Pennsylvania campus. Dao, who earlier in the day had fallen and slammed her kneecap on cement stairs, was hobbling on crutches. Gathered around a cafe table with their drinks, just across Locust Walk from the Wharton School, their conversation turned to their shared interest in the business side of health care.

Dao had completed her undergraduate degree at Penn the previous year. "Being at Penn, I've always had friends at Wharton and the nursing school and engineering," she says. "That cross-pollination shaped me so much. That was something I wanted to keep in my medical school education."

All three students had chosen to attend the Perelman School of Medicine (PSOM) because they were attracted to Penn's ecosystem of business and innovation. To them, medical education was about more than becoming a top-notch physician — though that was a key aim. It was also about finding a place in a rapidly evolving health care ecosystem, where fitness trackers and connected apps were flourishing, doctors were launching health-focused startups and medical providers were preparing for the mandatory shift to electronic health records.

The three classmates already had ideas they were eager to explore. O'Connor hoped to develop his own health care startups. Soegaard Ballester wanted to hone her skills in health informatics — the combination of health care and information technologies to improve patient outcomes. And Dao was intrigued by health care leadership and operations management. But without a structured avenue for early medical school students to access Penn's business community, the trio felt they were still on the outside looking in.

When they went their separate ways for winter break, Dao, Soegaard Ballester and O'Connor fleshed out their ideas in a shared Google document. They drafted a proposal for a new medical student group — initially called the Business and Technology of Healthcare — and an accompanying area of concentration in the medical school curriculum dubbed Healthcare Management, Entrepreneurship, and Technology (H-MET), which was modeled on other medical school concentrations, such as those in women's health and global health.

"By having these [business and technology] skills early on," O'Connor says, "we thought as we entered the wards and saw the world around us, we'd be able to get more out of medical school."

Ten years later, the program now known as PennHealthX has exceeded the expectations of its founders — and far surpassed the accomplishments of a traditional student club. HealthX has grown into an influential student-driven creative hub within the Perelman School of Medicine, a place where future doctors can experiment with new ideas at the crossroads of medicine and other disciplines, discover alternate career paths and even launch their own businesses. PennHealthX includes a popular lecture series, internship funding, an annual conference and a venture arm, as well as a revolving host of projects based on the interests of its student participants.

PennHealthX, as more than one alumna notes, is essentially itself a startup business in miniature. "It's a very entrepreneurial program in which the students really do drive it," says J.C. Lopez, MD'18, MBA'18, who after Dao became the second president of HealthX and is now a principal on the health care team of a venture capital firm. "You run it like a startup."

PSOM graduates with ties to HealthX are now innovating in every sector of health care. Some are practicing physicians, like Dao, who graduated from PSOM in 2017 with MD and MPH degrees, now a pediatric anesthesiologist, and O'Connor, a skin cancer surgeon in New Hampshire. Others, like Lopez, eschewed residencies to enter the world of health care investment. Some are continuing their study of the intersection of health care and business, like Soegaard Ballester, MD'17, MBMI'22, who is working toward her goal of building a career that includes both thoracic surgery and informatics. Others are developing their own startups.

And the ranks of PennHealthX alumni will only grow, as a \$6 million gift from health care investor Roderick Wong, MD'03, has endowed the program, ensuring it can continue in perpetuity. "You have leaders in clinical medicine and leaders in academic medicine, but [HealthX students] are

Pictured on opposite page: As vice presidents of strategy for PennHealthX in 2022, Angela Malinovitch and Danielle Brown led the student group's new Social Determinants of Health Accelerator program. Brown and Emily Xu, also a HealthX leader, both interned for a startup business focused on maternal health equity for Black mothers.

going to be the leaders in medical innovation,” Wong says. “It’s great that Penn is attracting those people because they’re going to change the future.”

Formation

The success of PennHealthX was not assured from the start-up phase.

In early 2013, when Dao, Soegaard Ballester and O’Connor pitched their proposal to the medical school administration, the H-MET area of concentration was met with skepticism. Why, school leaders asked, would a medical student interested in business choose this concentration over the university’s prestigious dual MD/MBA degree?

To Soegaard Ballester, the answer was clear. After the expense and time commitment of medical school, she says, adding another degree isn’t an option for everyone. Plus, the area of concentration would provide a broad scope of business content geared specifically toward future physicians on subjects such as funding and pricing new clinical therapies, health care system quality improvement, and making the leap from bedside to business.

The students approached David Asch, MD, MBA’89, and Shivan Mehta, MD’06, MBA’06, MSHP’12, leaders of Penn Medicine’s then-newly established Center for Health Care Innovation, for guidance. Asch, now senior vice dean for strategic initiatives at the medical school, was struck by the suite of initiatives dreamed up by the trio to advance the concept and deployment of “a new lane in academic medicine.”

“It was the students who saw both the need and the opportunity,” Asch says. “In every way, this was created by the students and for the students and reflects the students advancing the Perelman School forward.”

While most people who earn a medical degree go on to become practicing physicians, Asch says, the variety of careers for those who don’t go into practice is immense. “I don’t think a medical degree is any less versatile than a law degree,” he says. “There are many ways to get medical training and use it to advance health and health care. [HealthX] is an illustration of that.”

Validation

The trio of co-founders reshaped and strengthened their proposal, and on the second try, PennHealthX and the H-MET area of concentration (dubbed a “certificate” at that time) were approved.

But by that time, Dao, Soegaard Ballester, and O’Connor only had six months until they were to begin their clerkship year of intensive hands-on clinical training, when they knew they couldn’t continue leading the group effectively. So as they were building their new program from the ground up, they were also preparing for it to go on without them.

They began recruiting newly admitted medical school students to join HealthX and established a six-month board, as well as the next board to lead the group when the founders were on rotations. “We made sustainable leadership structures and mentorship cornerstones of the program,” Soegaard Ballester says, “because without that it would just fall apart in a year.”

At the same time, PennHealthX began hosting lunchtime lectures on the intersection of health care and business, drawing speakers from Penn’s faculty and the medical school’s alumni pool. (Attendance at these lectures was — and still is — a core requirement of the H-MET area of concentration, along with certain required courses and an internship or research experience.) Asch was an early and frequent HealthX speaker, along with Wong, who traveled from New York to talk about his work as a biotechnology investor and founder of the firm RTW Investments.

Egen Atkinson, MD’16, MBA’16, remembers attending Wong’s talk. Although Atkinson had worked at a biotechnology company before enrolling in medical school, he was rapt hearing Wong describe his work. As an investor, he uses his medical knowledge to evaluate which drugs are most worthy of investment, and to select the projects that have the greatest chance of offering significant help to the greatest number of people. “I thought that was the coolest thing I’d ever heard,” Atkinson says.

Today, Atkinson and fellow alumnus Michael Kramarz, MD’15, MBA’15, draw on their medical science backgrounds to run Commodore Capital, a biotechnology investment firm that specializes in funding small companies developing therapeutics in oncology, neurology, autoimmune diseases, and other clinical areas. “In medical school, most of your peers will go on to be clinicians and researchers, which is how it should be,” Atkinson says. “But the world does need people with medical and business training to do other things. It was wonderful to have a program that opened the door and showed what was possible.”



B.A. Sillah, MD’17, MBA’17, has built a career in health care investing based on experiences and opportunities he seized through PennHealthX programs in medical school.

Along with attending PennHealthX lectures, students interested in earning their degree with the H-MET area of concentration are required to complete an internship or research experience. For B.A. Sillah, MD’17, MBA’17, that internship turned out to be his first direct involvement in the world of health care investing. Sillah spent the summer of 2015 at the Nairobi health care investment firm of a Wharton alumnus studying how investors supported health care innovation.

But the internship likely wouldn’t have happened without HealthX. Sillah says he got the gig by keeping in touch with the alumnus, who had been a guest speaker for a class on global health. He credits HealthX with instilling in him the importance of networking and relationship building. “HealthX taught the importance of structuring and maintaining a community in this space,” Sillah says. “So much of venture capital, so much of biotech, is driven by the community you create and maintain.”

When he learned the opportunity was unpaid, Sillah again turned to HealthX, which used some of its modest budget to help medical school students fund business-related internships. Sillah applied for funding, and HealthX offered him a stipend, plus additional support for expenses.

That internship set the trajectory for his career since. “It put me over the edge to decide that I wanted to go the non-clinical route and go into health care investing,” says Sillah, who today is chief operating officer of Avesta76 Therapeutics, a biotechnology company that develops cancer medicines, and is helping a New York bank establish a venture capital arm.

Fundraising

Within a year of the establishment of a HealthX board structure, the group had developed an ambitious vision for what their program could become and sought to boost their \$5,000 budget to turn their “pie in the sky” dreams into reality.

They had applied for internal funding at Penn and other grants, and they didn’t stop there.

On an August day in 2014, J.C. Lopez boarded an Amtrak train to New York City with Lisa Katz, director of leadership gifts at the Perelman School of Medicine. Lopez was then beginning his second year of medical school and was six months into his term as president of HealthX after the founders began clerkship rotations that January. He and Katz were headed to Wong’s Manhattan office to “pitch” PennHealthX as a potential investment opportunity.

Toting a business plan, printed slide deck and budget, Lopez told Wong, who was already familiar with the HealthX lecture series as a speaker, about the program’s other offerings, including a healthcare-focused hackathon the group was planning for the following month to attract Penn students interested in creativity and entrepreneurship.

Lopez was happy with his pitch, though he didn’t expect anything to come of it. “It was a fun day,” he says. “I really enjoyed meeting alumni who were doing things that, at the

time, I didn't even realize I wanted to do in my future career."

Less than a month after Lopez and Katz's visit, Wong signed a \$300,000 gift agreement to fund PennHealthX for three academic years. "It's attracting those visionary types of students," he says. "They want to help each patient today, but they also want to make medicine for patients in the future better."

Wong became an involved benefactor to HealthX. He helped solidify the group's institutional memory by suggesting a structure that encouraged previous HealthX board members to return to as advisers after their clerkship year. Now, the HealthX board is most often composed of fourth-year medical students in co-president positions, along with a group of first- and second-years as vice presidents of strategy, curriculum, entrepreneurship and other areas.

Lopez, for instance, rejoined the board in 2017 when he had completed his clerkship and entered Wharton's MBA program. Along with overseeing junior board members, Lopez returned to HealthX with a new program idea. "What I was learning in business school was very useful and some of it could be distilled down," he says. "That's when HealthX

Combining her background in materials engineering with her medical degree, Tiffany Yeh, MD'22, opted not to pursue a residency. Instead, she is launching a startup business designing cold therapy wearables.

started a seminar series with more structured programming around accounting, or finance or marketing — aspects that are relevant if you were to go into hospital administration or other areas."

In 2017, Wong decided to fund HealthX for three additional years. He also established a scholarship fund to support PSOM students who want to pursue a Wharton MBA.

Growth

PennHealthX held its inaugural conference, now a marquee annual occurrence, in 2016.

Leaders in medical entrepreneurship and innovation came from all over the Philadelphia area to be part of the daylong event titled "MD as a Passport." Moderna's then-chief financial officer Lorence Kim, MD'00, MBA'00, and former Christiana Care Health System chief executive Robert Laskowski, BA'74, MD'78, MBA'83, gave keynotes. Wong traveled from

David Mui, who will earn MD and MBA degrees from Penn this spring, helped build connections between PennHealthX and other institutions during his tenure as the group's co-president with Tiffany Yeh.

New York to present an investment case pitch, walking a group of about 20 students through his thought process on an example investment.

The conference, like PennHealthX programming lineup overall, was increasingly providing an accessible avenue for medical students interested in the business side of health care to get exposure to the players, internships, alumni and opportunities in the industry, Lopez says. (Lopez himself was hired at the firm New Enterprise Associates by a HealthX speaker, Ali Behbahani MD'08, MBA'08, after they forged a relationship over their shared interests.) "Our philosophy was that every doctor should be aware of these skills and, at a high level, understand how they operate and how they affect their lives and the lives of their patients," Lopez explains. "We're trying to increase the catchment area."

It worked. PennHealthX was getting noticed, especially within the medical school. In a 2017 survey of 351 PSOM students by the HealthX team, 79 percent of respondents said they'd attended at least one HealthX event. More than one in five said the existence of HealthX — a rarity among medical schools — influenced their decision to attend PSOM. And a full 11 percent of respondents changed their career paths because of their participation in HealthX.

In addition to receiving funding for unpaid internships through HealthX, medical students could by then take

advantage of the HealthX venture fund. The fund, which continues today, has provided non-dilutive seed funding to more than a dozen student-run businesses.

PennHealthX also nurtured new ideas for its own programs. Ryan O'Keefe joined PennHealthX as a first-year medical student in 2016 in the way typical for new participants: He began attending the group's popular lunchtime lectures. But O'Keefe, who also had an interest in audio communication, quickly noticed a missed opportunity. "We have these amazing speakers coming to our campus — doctors or business people within the Philadelphia and Penn community, and outside of it," he says. "Even though we would have an excellent turnout of 60 or 80 people sometimes, I felt it was a shame it was limited to the students who could be there in person."

O'Keefe proposed a PennHealthX podcast featuring interviews with the speakers who came to campus sharing their insights and career takeaways. The HealthX board saw the podcast as an opportunity to "think big" (one of their marching orders from Wong) and further extend the group's growing reach from the medical school to the rest of the Penn campus and beyond. Guests included David Fajgenbaum, MD'13, MBA'15, an assistant professor of Medicine at PSOM whose remarkable story of becoming a rare disease specialist to save his own life had recently been covered in the *New York Times* and former medical school dean Arthur Rubenstein, MBBCh, who was instrumental in reshaping the culture of Penn Medicine. "You just don't get the opportunity to have those one-on-one conversations naturally," O'Keefe says.





Benefactor and health care investor Roderick Wong, MD'03 (second from left), poses with PennHealthX co-founders Diane Dao, MD'17, MPH'17, Dan O'Connor, MD'17, and Jacqueline Soegaard Ballester, MD'17, MBMI'22.

"All those things looked great," Wong says. "But what I didn't anticipate, the icing on the cake, was that [HealthX] had these 'butterfly effects' as a model." Since PennHealthX was formed, other medicine-plus groups and efforts have launched to connect PSOM students with their other shared interests outside medicine. Examples include the Penn Med Symphony Orchestra, which formed in 2016 and is open to medical students, and the Arts and Medicine student group, which held its first show of student art in 2018.

That's a trend in keeping with what Suzanne Rose, MD, MSEd, senior vice dean for medical education at PSOM, says she wants to see — helping students to individualize their medical education based on their interests. "My goal is to create leaders and do-gooders," Rose says. "Whether the students want to be clinician-scientists, work in advocacy, in politics or in business, they should always be thinking about the patients and the communities served by what they do."

In November 2019, Wong signed a \$6 million endowment gift to fund PennHealthX in perpetuity. The endowment

"You have leaders in clinical medicine and leaders in academic medicine, but [PennHealthX students] are going to be the leaders in medical innovation."

— Roderick T. Wong, MD'03

was one of the largest single gifts to support medical education at PSOM. "We ran the experiment. The students proved its value," Wong says. "We wanted to make sure HealthX didn't have to worry about permanence."

Four months later came COVID-19.

As medical students adjusted to a new world — and did their best to help during the unprecedented health emergency — Alex Beschloss, MD'22, MBA'22, then HealthX co-president with Elana Meer, MD'22, MBA'22, says he realized the pandemic was the next inflection point for the student group. "We saw how COVID-19 ravaged the world, disproportionately affecting those who have poor access to many structural and social determinants of health," he says. "I realized HealthX had a unique opportunity to make an impact while also helping expose Penn Med students to the business strategy world."

Beschloss designed the PennHealthX "social determinants of health accelerator," an initiative that pairs HealthX students with startup businesses geared toward solving public health problems. In its initial iteration, the accelerator connected three startups — one focused on maternal health disparities and the other two on food insecurity — with six medical student interns who could offer support at no cost to the startup. "While HealthX absolutely still explores areas of innovation around health tech, business, management and biotechnology," Beschloss says, "the accelerator added increased focus on how these topics can be applied toward equity and access to health care."

Some social determinants of health accelerator participants are now interning with Tiffany Yeh, MD'22, who recently completed her term as HealthX co-president. Yeh, who has a background in materials engineering, opted not to pursue a medical residency in favor of founding her own health care startup business. Inspired by Yeh's own chronic health condition, Eztia is a company that designs discreet and convenient cold therapy wearables for athletics, women's health, and other consumer health applications. "As a solo founder, building a talented and dedicated team is all the more crucial," she says. "Penn medical students have been working with me on translating clinical knowledge

into educational content around the mind-body connection, pain and women's health."

A key part of Yeh's recent tenure as PennHealthX co-president along with fifth-year MD/MBA student David Mui was building interconnectedness between HealthX and similar groups at other institutions. Last year, a group of HealthX students pioneered the inaugural "Boston Biotech Trek," traveling to New England's medical hub to meet with industry leaders from Harvard, the Massachusetts Institute of Technology and other institutions. "[HealthX] will continue to push forward new, innovative ideas that are relevant to the health care system today," Mui says.

Despite graduating from medical school last May, Yeh says she was happy to stay on for another few months as HealthX co-president. "In medical school, you've got this [classroom learning] period and then you go into the hospital and you drop off the face of the Earth," she says. "But what I find so interesting about HealthX — and the Penn community in general — is that people come back. You don't lose those parts of your identity. You come back to nurture that and keep the thread going."

Lamin Sonko, MD'22 MBA'22, is one of those who have continued to expand his view thanks to his time in HealthX, which included serving as vice president for innovation. Now a Penn Emergency Medicine resident, Sonko is passionate about using his skills to help build health care infrastructure in sub-Saharan Africa.

"Being on the MD track forces you in some ways to be somewhat narrow-minded in terms of not only career opportunities, but opportunities in health care," he says. "Clubs like HealthX really help shift that paradigm and show there are lots of different innovative ways to improve health care outside of seeing patients."

"We're already seeing this, but it's only going to be more obvious," Yeh says, "that you will have Penn Medicine alumni literally in all of the different facets of business and tech and medicine that you can possibly think of." ☐

Read this story online with related links at PennMedicine.org/magazine, and read more about the PennHealthX SDOH Accelerator at Service in Action, CommunityImpact.PennMedicine.org.

All told, the podcast garnered more than 40,000 listens before it ended after 78 episodes. (One of those listeners was Jonathan Wakim, who discovered the HealthX podcast as a college junior and decided he wanted to go to medical school at Penn. Once enrolled, he immediately joined HealthX and is now a co-president.)

Though O'Keefe, who graduated with an MD and MBA in 2021 and is now an internal medicine resident at the Hospital of the University of Pennsylvania, would have liked the podcast to continue, he acknowledged that, unlike the core programs of PennHealthX, side projects such as the hackathon and podcast eventually run their course. That's what's so great about a program like [HealthX]," he says. "People have their pet projects they bring to life. [They become] different products, just like you'd find at an innovative company like Google. You see what works. You put it out there and if there's a desire to keep it going, then it will keep going."

Scaling

In 2019, as Wong's second three-year round of funding was nearing its end, PennHealthX reached an inflection point.

It was time for Wong to decide how he might continue to support the program. Just as he does with his business investments, Wong pored over the numbers, looking at statistics on overall interest in HealthX, conference attendance, H-MET concentration sign-ups, podcast listens and more.

VERY PERSONAL CARE — MADE POSSIBLE BY VERY PERSONAL PHILANTHROPY

Rare diseases are a puzzle for the scientists and clinicians who study and manage them — and the patients suffering from them too. Take Sweet syndrome: an inflammatory disorder in which a patient’s neutrophils (a type of white blood cell) attack their own skin as if it were an infection. Challenging to diagnose and treat, Sweet syndrome looks and responds to treatments differently from patient to patient, requiring constant innovation and creativity.

For one Sweet syndrome patient at Penn Dermatology, the clinical team — including her physician, Misha Rosenbach, MD — wanted new options for her care. Although she had been treated with corticosteroids that controlled her Sweet syndrome at high doses, the side effects were devastating. She had been hospitalized four times in only two years for flares of her disease.

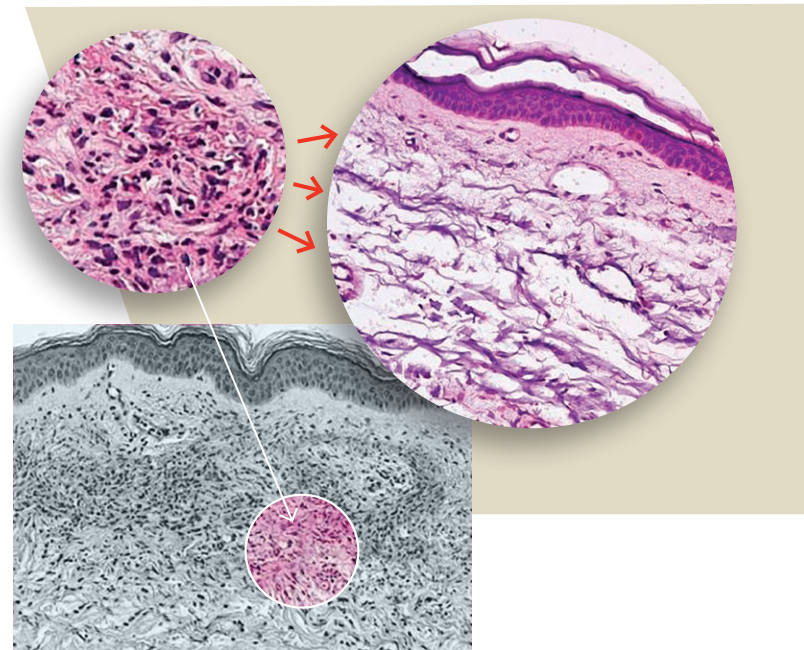
Due to the complex and personalized nature of Sweet syndrome, Rosenbach felt she would respond best to a targeted treatment: one that could control her neutrophilic inflammation with fewer side effects. Discovering such a treatment would be possible only with the momentum of an entire team.

The Translators of Insight into Individualized Care

To investigate this approach, Rosenbach, an associate professor of Dermatology in the Perelman School of Medicine, turned to his partner in the department’s translational research program, Thomas H. Leung, MD, PhD. A collaborative comprised of Leung, Rosenbach, Robert G. Micheletti, MD, and William James, MD had been studying patients with neutrophilic diseases such as Sweet syndrome to find consistent patterns underlying the disorders: mutations, signals, or other factors that might explain the origin of Sweet syndrome in some — or all — of their patients.

Together, they conducted genomic profiling of this single patient’s samples, and found something electrifying: a mutation in her neutrophils had caused increased production of the receptor to IL-1, a well-established inflammatory signal. This change encouraged her neutrophils to migrate more readily and drove her clinical symptoms.

Back in the clinic, Rosenbach found that treating the patient with a targeted therapy blocking IL-1 resulted in complete remission of her Sweet syndrome and enabled



her to taper off her corticosteroids for three years (and counting!). Her life was transformed: no more side effects, symptoms, or hospital stays.

Taking insights like these from patients into the lab — and then translating them into action to guide therapy — requires the kind of seamless collaboration between scientists and clinicians that is a cornerstone of Penn Medicine. “Our partnerships with Dr. Rosenbach and other clinicians are prime examples of how Penn Dermatology facilitates research translation,” Leung notes. “To offer a successful new therapy to even one patient is incredibly motivating and is the first step to revolutionizing care.”

The research team’s insights were published in the *Journal of Clinical Investigation* last November. Already, this case has inspired similar research studies for two additional rare skin disorders. Because rare diseases like Sweet syndrome often affect critical body functions, further studies will improve our overall understanding of genes and biology, inspiring a “halo effect” of research.

“We are eager to lead personalized medicine approaches for our patients at Penn Dermatology, to match patients with effective targeted therapies that treat their disease with the fewest side effects,” notes Rosenbach.



Jerry and Joan Berstein

A Crucial Family Partnership

For the Sweet syndrome team, support from the Berstein family has been fundamental to their ability to conduct this personalized medicine-based research.

When Joan Berstein first sought a diagnosis for her skin disorder, she was dismayed by the lack of answers. Her diagnosis was “trial and error,” according to son Jeff Berstein, and required input from dozens of experts. She would joke she had seen a hundred doctors before her eventual diagnosis of Sweet syndrome at Penn Dermatology in 2012.

Far from allowing the complexity and rarity of her disorder to deter her, Joan became a staunch advocate for her fellow Sweet syndrome patients. She formed a close partnership with William James, MD, her primary clinician, and quickly came to realize the essential need for research funding for this rare disorder.

“She recognized that rare disorders like Sweet syndrome don’t get a lot of funding, and many people aren’t even aware they exist. [My parents] felt that there was a deep need for other patients like her to have hope for new treatment options,” Jeff Berstein says. Joan and her husband, Jerry, made their first contribution to Penn Dermatology’s Sweet syndrome research program in 2015.

Though Joan passed in 2020, she left a legacy that will impact the lives of countless Sweet syndrome patients — and more, as research insights contribute to biological understanding in other diseases, too.

Behind Every Therapy, A Team

In studying rare diseases, all types of collaborators — from patients to donors, basic scientists and clinicians — hold a piece of the puzzle. As a vital part of the team, the Berstein family meets regularly with James and the Sweet syndrome researchers to hear about their steady progress. Joan would always attend these updates, equal parts rapt attention and enthusiasm; now, it’s become a family affair, with Joan’s grandchildren present at the latest research update last fall.

“Who else can better understand the urgency of this work than our patients and their families?” James says. “Our patients contribute in so many ways: through time in clinic, participation in studies and trials, samples for our biobank, and even funds to launch new projects. Joan has been such a committed partner and she and her family are a major part of the progress we’re making now.”

“[My mother] would be so thrilled to see the progress right now,” Jeff says. “She really felt she was making a difference.” Thanks to the Berstein family’s support, the team has published five more studies across a host of related diseases, termed “neutrophilic dermatoses,” with more on the way.

Philanthropy: The Piece That Makes Progress Possible

Because of the speed required of personalized medicine, some of the most vital partners in the puzzle of rare diseases are Penn Medicine’s community of donors who contribute funds to accelerate research timelines. Traditional sources of support, such as government grants, can take three years from submission to funding — time which makes innovative, early-stage investigational work harder to get off the ground. Philanthropy, by contrast, provides flexible, immediate resources to open new avenues of investigation.

To learn more about supporting Penn Dermatology and personalized medicine for rare diseases like Sweet syndrome, reach out to Caitlin Crowe Doelp at 215-746-2167 or ccrowe@upenn.edu.

GROWING A PENN MED FAMILY BOUND BY SERVICE

It's not often that someone comes from as much of a medical family and Penn legacy as Joan MacCracken, M'71. Joan MacCracken has grandparents, uncles, parents, cousins, and nieces and nephews with ties to Penn and the Perelman School of Medicine going back more than a century. "My family gave me tremendous role models," she said, "and they also instilled a love of Penn that I was later able to live firsthand."

While she followed in her family's footsteps, graduating from the Perelman School of Medicine in 1971, she chose to carve out her own expertise, eventually caring for Navajo people through the Indian Health Service (IHS). That experience changed her life and the trajectory of her career. She went on to become a pediatric endocrinologist, caring for people in remote areas like Bethel, Alaska and northeastern Nicaragua.

On the occasion of her 50th Reunion, MacCracken established the McCracken/MacCracken (McMac) Student Travel Award for Indigenous Health — creating an opportunity for Penn medical students to challenge their cultural biases, familiar surroundings, and medical aptitude. The McMac Award provides financial assistance to two final-year Perelman School of Medicine students participating in educational and experiential learning at Indigenous health sites in the United States.

"Perelman School of Medicine students receive really crucial experience caring for a variety of populations in and around Philadelphia — a city that is home to a very diverse collection of people from all over the world," she explains. "But one group of individuals that students and physicians in Philadelphia do not see regularly are those of indigenous



Because the McCracken/MacCracken family's service was at the center of their medical careers, the McMac Student Travel Award opens the door to similar, meaningful opportunities for Perelman School of Medicine students.

descent. While every tribe is different and every individual person is very different, having clinicians who understand common health conditions that indigenous people face, and who understand their specific cultures, is imperative."

For This Family, There's Quite a Bit in a Name

In creating the Award, MacCracken drew inspiration from two major figures — and names — from her family tree. Her med school yearbook contains a dedication to her grandfathers: Josiah C. McCracken, M'1901, and Henry Noble MacCracken.

While at Penn, Joe McCracken was an All-American guard in football and also excelled in track and field, breaking the world record in the 16-pound hammer throw in 1898 and earning two Olympic medals in 1900 in Paris. He went on to be a dedicated medical missionary in China for more than 35 years. In 1906, the University of Pennsylvania Christian Association asked him to visit Canton and explore the potential to develop a medical school at that location. After seven busy years in Canton, he moved to Shanghai to become dean of a newly combined University of Pennsylvania Medical School at St. John's University.

"When we talk about global health, we often think that we need to travel halfway around the world," his granddaughter Joan MacCracken says. "But there are unique experiences and important work that we can do here in the States."

In creating the McMac Award, she notes the reciprocity of the learning experience. "The IHS, in general, is very good about meeting people where they are and specifically targeting care for their patients. Whether that is through at-home visits to remote areas for assessments and vaccinations or incorporating traditional medicine and individuals' beliefs with western medicine, clinicians really take a whole-person approach to medicine. They also are great problem solvers."

► **If you would like to contribute to the McCracken/MacCracken (McMac) Student Travel Award for Indigenous Health — or discover how you can impact medical education in a way most meaningful to you — please contact Kathleen Margay at 215-873-3793 or kmargay@upenn.edu.**

THE ABILITY ACADEMY: A PARTNERSHIP FOR AUTISM-INCLUSIVE PRESCHOOL

As Founder and Board Chair of The Helix School for students with autism spectrum disorder, Marjorie McMorris and her husband, Penn Trustee Marc F. McMorris, C'90, WG'94, understand that education partnerships are essential for giving all children a strong foundation in life. In 2014, they teamed up with Drs. David Mandell and Robert Schultz to launch the McMorris Autism Early Intervention Initiative, which funds pilot research initiatives and the McMorris Fellows: junior faculty, postdoctoral Fellows, doctoral students, and undergraduates who lead those projects. Today the McMorris Fellows are using new tools — including artificial intelligence to analyze speech, facial expressions, and other nonverbal communications — to identify potentially successful interventions.

The McMorrises followed that with a leadership gift to advance a bold vision for an inclusive preschool that builds on Penn's success as the world's premier site for conducting community-based studies on autism intervention and a more than decade-long partnership with the School District of Philadelphia.

When fully operational, the Ability Academy at Penn will be able to meet the needs of 225 children, offering both full- and half-day preschool. A long-term goal is to train and support Philadelphia School District staff and community-based preschool and daycare providers in effective, inclusive practices, ensuring that the community is better prepared to serve children with autism. The Academy will also train the next generation of educators, researchers, and clinicians, including Penn students from undergraduates to postdoctoral fellows.

As Mandell, a professor of Psychiatry and Pediatrics at Penn, explains, "If we can create a new model through our partnership with the Philadelphia School District — the nation's eighth largest — imagine the impact we will make nationwide."

Inspire With Your Impact: Support the Ability Academy at Penn

University of Pennsylvania Health System (UPHS) CEO Kevin B. Mahoney has been a formidable champion for the project, including offering matching gifts from UPHS. "The Ability Academy's commitment to working with the community



and bringing evidence-based care to autistic children represents the very best of our institution," he says.

Philanthropic donors can now help bring this vision to life. Naming gift opportunities include the Academy's playground, kitchen, and STEM classroom.

Gifts also can help grow the students' interdisciplinary care teams through the Parent and Caregiver Training Program. The Academy will provide tuition assistance for families of typically developing students; philanthropic support will be central to maximizing that access. The Academy also could benefit from social impact investing by those interested in strengthening the educational, social, and economic framework of West Philadelphia.

► **By giving all children a strong foundation rooted in acceptance, encouragement, and active engagement, the Ability Academy at Penn will foster the growth of life-long learners and compassionate citizens. You're invited to contact Paige O'Malley at 267-838-0660 or pomalley@upenn.edu to learn more.**

Send your progress notes and photos to:
Donor Relations
Penn Medicine Development and Alumni Relations
3535 Market Street, Suite 750
Philadelphia, PA 19104-3309
medalum@dev.upenn.edu

1960s

Edward Bluth, BA'67, MD, GME'75, has received the 2023 Gold Medal of the American College of Radiology (ACR), which will be awarded on May 7. The ACR Gold Medal is awarded by the ACR Board of Chancellors to an individual for "distinguished and extraordinary service to the ACR or to the discipline of radiology."

1970s

Don Pathman, BA'76, MD'81, of Durham, North Carolina, and **Jim Glickson, BA'76**, of New York, bicycled from Buffalo to Albany, New York in September along the 365-mile-long Erie Canalway Trail. They write, "This ride was almost 50 years to the day that we first met in the Lower Quad as freshmen. Although we biked considerably longer distances during our days at Penn and shortly thereafter, as two 68-year-old bikers, we were nevertheless quite pleased with ourselves, thank you. We're already planning our next trip."

1980s

Helene D. Gayle, MD'81, was inaugurated as the 11th president of Spelman College and began her presidency on July 1. Spelman College is a historically Black, private liberal arts and sciences college for women.

David J. Shulkin, MD, GME'86, has been appointed to the new iXlayer Health Testing Advisory Board (iHTAB), announced on



Helene D. Gayle, MD

Nov. 1. The iXlayer Health Testing Advisory Board consists of industry leaders and experts who will serve as thought partners and strategists to further the movement of making health testing more accessible and affordable.

1990s

Angela DeMichele, MD, GME'92, GME'94, GME'98, GME'01, a professor of Medicine and Epidemiology at Penn and co-director of the breast cancer program at Penn Medicine's Abramson Cancer Center, has been named a 2022 Founders Honoree at the Living Beyond Breast Cancer Butterfly Ball.

Jennifer Moriatis Wolf, MD'95, a professor of Orthopedic Surgery and Rehabilitation Medicine at the University of Chicago, has been appointed president of the American Society for Surgery of the Hand. She is the second woman to hold this position.

OBITUARIES

1940s

Edgar E. McCannless, MD'49, a pediatrician; Aug. 15. McCannless served in the United States Air Force. While studying at the University of Pennsylvania, he was a member of the John B. Deaver Surgical Society and the Strecker Psychiatric Society. McCannless began working as a pediatrician

at Lake Charles (Louisiana) Medical Surgical Clinic, joined the Lake Charles Children's Clinic in 1980, and was one of the first doctors in the area to work with the Head Start Program.

1950s

Jonas Brachfeld, MD'52, GME'56, a cardiologist; Dec. 30. Brachfeld was a practicing cardiologist throughout his professional life and served on the medical faculty of The University of Medicine and Dentistry of New Jersey. Together with other newly trained Jewish physicians who were refused staff privileges at a county hospital in New Jersey, he founded Rancocas Valley Hospital (Willingboro, NJ) where he was the chief of staff for over two decades. He was also the founder and president of Brachfeld Medical Associates, also in Willingboro.



Stanley P. Mayers Jr., BA'49, MD'53, public health services officer; Jan. 3. Mayers' undergraduate studies at the University of Pennsylvania were interrupted by his U.S. Navy service during the Second World War. He subsequently returned and received both a Bachelor of Arts and a Doctor of Medicine at Penn in 1949 and 1953, respectively, followed by a Master of Public Health at Johns Hopkins University (JHU) in 1958. Mayers also completed an internship at Philadelphia General Hospital and a residency at the Arlington County (Virginia) Health Department. He was board certified in Preventive Medicine.

In 1955, Mayers was appointed health director for the Henry-Martinsville-Patrick Health District in Virginia, and later went on to become the regional director for the Virginia State Health Department and district state health officer for the New Jersey State Department of Health. From 1965 to 1971, he served as the director of the Arlington County Department of Human Resources in Northern Virginia. He also held appointments at the Georgetown University School of Medicine and JHU. From 1962 to 1965, he was the assistant dean of the JHU's School of Hygiene and Public Health.

In 1971, Mayers was invited to join Penn State University to help develop a new program in Health Planning and Administration, in what was formerly called College of Human Development. He chaired the department for nearly a decade and served as the associate dean for Undergraduate Studies and associate dean for Academic Studies of the College of Health and Human Development. His support led to the establishment of The Margaret A. and Stanley P. Mayers Memorial Scholarship and the Virginia L. Mayers Memorial Scholarship, as well as the Stanley P. Mayers, Jr. Health Policy and Administration Excellence Endowment.

He remained active as the vice chairperson of the Centre County Hospital Commission until 2021, continued to chair the Biomedical Review Committee at Penn State, and, for most of 2000, acted as the interim director of International Education Programs and Studies (Global Penn State). Mayers was a fellow of the American College of Preventive Medicine and of the American Public Health Association. He was also a past president of the Centre County Medical Society, and the Virginia chapter of the American Association of Public Health Physicians.

McHenry Peters Jr., MD'54, a radiologist; July 30. Peters served four years in the U.S. Army. He was a radiologist for 30 years, serving at several hospitals in the Wilmington, DE area. From 1977

to 1986, he was appointed by Governor Pierre S. du Pont IV to serve on the Authority of Radiation Protection of the State of Delaware. Peters received the Fellow of the American College of Radiology (FACR) honor in 1991.

Robert E. Weibel, MD'55, an immunologist; Sept. 29. Upon completing his pediatric medical residency at Children's Hospital of Philadelphia, Weibel served in the U.S. Army from July 1958 until July 1960, and then became a partner in a pediatric practice in Havertown, PA. After nine years in practice, Weibel accepted a position at Merck Sharp & Dohme as director for Virus and Cell Biology and then director of Experience and Epidemiology. He was instrumental in the clinical studies of vaccines for measles, mumps, rubella, chicken pox, and hepatitis B. He also held a joint position at the Perelman School of Medicine, teaching residents and new physicians in immunology. Weibel ended his career with the Health Resources and Services Administration in Rockville, MD where he served as senior medical officer for the National Vaccine Injury Compensation Program.

Robert Clare Bornmann, MD'56; Dec. 6. Bornmann served for 27 years in the U.S. Navy, including stations in Antarctica, the U.S. Navy Diving School, the Deep Sea Diving School, the Royal Naval Physiological Laboratory, and the Navy Medical Research and Development Command. He was the deputy medical officer for the U.S. Navy Deep Submergence Systems Project, working on SEALAB III and developed the protocols for saturation diving and decompression tables still used today.

Walter Dex, MD'56, a radiologist; April 11, 2022. Dex completed his internship and radiology residency at Philadelphia General Hospital. He was certified by the American Board of Radiology and awarded a fellowship in American College of Radiology. Dex was a Captain in

the U.S. Army and served as chief of the Radiology department at Fort Leonard Wood in Missouri from 1960 to 1962.

He served as chief of the Radiology department at Allentown Hospital from 1973 to 1989 and was a member of the Radiology department at Lehigh Valley Hospital from 1989 until retiring in 1996. He also served on the Board of Directors for The Allentown Hospital, Health East, Lehigh Valley Hospital, American Lung Association of the Lehigh Valley, and The Ethics Institute. He was a member of the Lehigh County and Pennsylvania Medical Societies, the American Medical Association, the Radiological Society of North America, and the Pennsylvania Radiological Society.

Margaret L. Garrett, MD'56, a psychiatrist; Oct. 30. Garrett graduated from the Perelman School of Medicine as one of only six women in her class. Upon completing her residency in New Haven, CT in 1968, she moved to Washington, DC, where she practiced psychiatry until retirement. Garrett was a fellow of the Washington Psychiatric Society.

Thomas R. Houseknecht, BA'52, MD'56, a psychiatrist; July 14. Houseknecht served in the Marines from 1946 to 1948, receiving an honorable discharge while holding the rank of corporal. He served as President of the New Jersey Psychiatric Association in 1976 and as New Jersey's representative to the Assembly of the American Psychiatric Association from 1976 to 1986. Houseknecht also served on the Burlington County Mental Health Board from 1986 until his retirement in 1994.

Hugh MacMillan Moss, MD'56, an ophthalmologist; Dec. 23. Moss served in the Army of Occupation in Japan from 1946 to 1948 as a paratrooper, Battalion Operations NCO (sergeant) in the 511th Parachute Infantry Regiment of the 11th Airborne Division. He completed his residency in ophthalmology at the Edward S. Harkness Eye Institute



of the Columbia University Medical Center and was recipient of a Visiting Heed Fellowship at the University of Oregon and the University of Iowa. In 1961, Moss was appointed to the faculty of Columbia University, teaching pediatric ophthalmology, ocular motility, and ptosis. He received the Knapp Teaching award for excellence in resident teaching. Moss was an attending physician at New York Presbyterian Hospital and past president of the Bergen County Ophthalmological Society, and had a private ophthalmology practice in Hackensack, NJ for 50 years.

Vardaman M. Buckalew Jr., MD'58, GME'62, a nephrologist; July 17. After completing his residency in 1962, Buckalew entered the U.S. Navy as a medical officer at the Naval Hospital in Newport, RI. He served at Wake Forest University's School of Medicine for 38 years in the departments of Internal Medicine and Physiology. Buckalew also served as chief of the section on Nephrology for 26 of those years, and four years as chief of Professional Services at Wake Forest Medical Center (Winston-Salem, NC).

Joseph A. Neal, MD'59, GME'64, a physician; Oct. 24. After earning his medical degree, Neal joined the U.S. Air Force, where he served with distinction for 30 years and retired at the rank of Colonel.

Donald S. Robinson, MD'59, a pharmacologist; Sept. 16. Robinson served in the U.S. Army during the Korean War. He completed his internship at U.S. Public Health Service Hospital in Seattle and his family medicine residency at Ventura County

(California) Hospital. Robinson also completed an internal medicine residency and a fellowship in hematology at Mary Fletcher Hospital, University of Vermont (UVM) College of Medicine, and practice hematology there for several years.

In addition to several professorships, he established UVM's division of clinical pharmacology and the department of pharmacology at Marshall University School of Medicine in Huntington, WV. Robinson became director for central nervous system drug development at Bristol-Myers Squibb, with global responsibilities, and shepherded three new medicines through clinical development to FDA approval before retiring in 1993.

1960s



Stanley Baum, MD, GME'61, chair of Radiology; Oct. 15. After completing his residency at Pennsylvania, Baum remained at the University as an associate professor of Radiology. He became chair of the Radiology department in 1975 and served until 1996. In 1977, Baum was named the Eugene P. Pendergrass Professor of Radiology. In 2001, Penn established the Stanley Baum Professorship of Radiology in his honor.

Robert J. Lenar, MD'62, an internist; Dec. 27. Lenar's career as a doctor of internal medicine spanned decades and included the position of chief of Staff at North Broward Medical Center. He also served as a Captain in the Air Force.



Edward J. Stemmler, MD'60, GME'64, dean emeritus; Jan. 3. After earning a bachelor's degree from La Salle College in 1950, Stemmler served at the rank of Sergeant First-Class with the U.S. Army's 401st Chemical Service Intelligence Detachment in Korea. He returned from the military in 1953 and entered the Perelman School of Medicine. Stemmler completed an internship and residency in Medicine and a

fellowship in Cardiology at the Hospital of the University of Pennsylvania (HUP) followed by a postdoctoral NIH fellowship in Pulmonary Physiology in Penn's Graduate Department of Physiology.

In 1964, he was appointed as an instructor in Medicine and was promoted to the rank of professor in 1974. In 1981, Stemmler was named the first incumbent of the Robert G. Dunlop Professorship in Medicine. He served

for two years as the chief of the Medical Outpatient Department of HUP and for six years as chief of Medicine of the University Medical Service at the VA Hospital in Philadelphia, a service that he established in 1966.

Stemmler served as associate dean for HUP in 1973 and associate dean for Student Affairs from 1973 until 1975. He was appointed acting dean of the University of Pennsylvania School of Medicine in 1974 and dean in 1975. Stemmler led the establishment of the Clinical Practices of the University of Pennsylvania and the Clinical Educator Faculty track. He also led the development of academic and institutional planning systems, which helped the School of Medicine prosper. In 1988, Stemmler resigned as dean to assume the full-time role of executive vice president, charged to create a new entity, the University of Pennsylvania Medical Center. He served as the head of the Center until 1989, when he was named dean emeritus by the University Trustees. In 1990, Stemmler retired from Penn when he assumed the position of executive vice president of the Association of American Medical Colleges (AAMC) in Washington, DC; he retired from the AAMC in 1994.

Stemmler served as a member of the National Advisory Committee to the Robert Wood Johnson Clinical Scholars Program and its Generalist Initiative, and as a member of the Advisory

Committee to the Director of the National Institutes of Health. He was a past chairman of the Assembly of the AAMC and a Distinguished Service Member of that organization, as well as a past chairman of the Board of the National Board of Medical Examiners of which he was named a Distinguished Service Member. Stemmler retired from the Board of Rhone-Poulenc Rorer Pharmaceutical Company in 1996 and from the Dorothy Rider Pool Health Care Trust in 2000, but he continued to serve on the Board of the SAW Community Foundation until 2005 and the Board of the AHC Community Foundation until 2008. He was a treasurer emeritus and master of the American College of Physicians, a member of the Institute of Medicine of the National Academy of Science, and a past president and member of the American Clinical and Climatological Association.

Stemmler received honorary degrees from Ursinus College, La Salle University, Rush University, the Philadelphia College of Pharmacy and Science, the Medical College of Pennsylvania, the State University of New York Upstate Medical University at Syracuse, and Georgetown University. He was a recipient of Lifetime Achievement and Distinguished Graduate Awards from the Perelman School of Medicine. A painting of Dr. Stemmler hangs in the ground floor of his namesake Stemmler Hall at Penn.

Robert S. English, MD, GME'63, a dermatologist; June 8. English graduated from the Hahnemann University Medical School, completing his residency in dermatology at the Perelman School of Medicine. For more than 50 years, he practiced dermatology both in Morgantown, WV, and in White House, PA.

Morris Z. Gardner, MD'63, a radiologist; Jan. 14. Gardner served as a Captain in the U.S.

Army from 1964 to 1966 at the 97th General Hospital in Frankfurt, Germany. He spent most of his medical career as the head of the Radiology department at Central Medical Center and Ellwood City Hospital in Ellwood City, PA.

Robert E. Ribbe, MD'63, an orthopedic surgeon; July 10. Ribbe began his medical practice in the U.S. Army with an internship at Madigan Army Hospital in

Tacoma, WA, and completed a residency in general surgery in Ft. Knox, KY, followed by a residency in orthopedic surgery at Tripler Army Hospital and Shriners' Children Hospital in Honolulu, HI. During the Vietnam War, he deployed to the 311th Field Hospital where he served from 1968 to 1969.

Ribbe then practiced at the West Point (NY) Army Hospital. Ribbe served as active senior staff of orthopedic surgery for Butterworth

Hospital in Grand Rapids, MI from 1971 until his retirement in 1994.

Malcolm Rourk, Jr., MD'63, a pediatrician; Sept. 4. A Fulbright scholarship recipient, Rourk spent a year in Germany studying and conducting research. After graduating from the Perelman School of Medicine, he became a Captain in the U.S. Air Force, serving from 1965 to 1968 at Eglin Air Force Base. Rourk

completed his residency in pediatrics, followed by a fellowship in pulmonology, and spent a sabbatical year at UNC Health (Chapel Hill, NC) where he studied pediatric gastroenterology. He spent his career as a physician at Duke University School of Medicine as an associate clinical professor, where he led the team that created the Division of Pediatric Gastroenterology and Nutrition. Rourk completed his career as the director of the Pediatric Residency Program, and served on the medical school's Admissions Committee for many years.

William H. Simon, MD'63, GME'67, an orthopedic surgeon; Sept. 11. Simon was trained, practiced at, and taught within the University of Pennsylvania Health System. He furthered his training at Harvard University and then practiced medicine in Philadelphia for the remainder of his life. During the Vietnam War, Simon served as a Lieutenant Commander with the U.S. Public Health Service at Walter Reed Army Medical Center and other hospitals. Additionally, he conducted published research at the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

Barry R. Zitomer, MD'63, an internist; July 20. After earned his medical degree from the Perelman School of Medicine, practiced internal medicine for more than 50 years in Morristown, NJ.

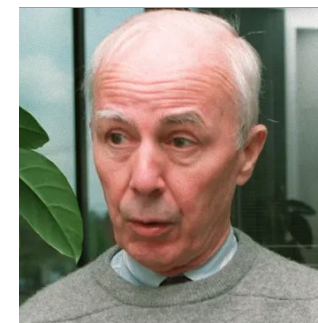
Sayre K. Jacobson, BA'60, MD'64, a cardiologist; Sept. 14. Jacobson served in the U.S. Army as a doctor during the Vietnam War, earning a Bronze Star for meritorious service. He practiced cardiology and internal medicine in Maplewood, NJ from 1971 until his retirement in 2015. Jacobson was a fellow of the American College of Cardiology and served for a time as chief of the Cardiology Section at St. Barnabas Hospital in Livingston, NJ and as an assistant clinical professor at Mt. Sinai School of Medicine.

Gregory O. Walsh, MD'64, GME'67, a neurologist; July 26. Walsh was a professor of Neurology at the University of California, Los Angeles (UCLA). After receiving his medical degree from the Perelman School of Medicine, he embarked on research at the NIH. As a UCLA Professor of Neurology, Walsh founded The Epilepsy Monitoring Program.

Vernon W. Morgan Jr., MD'65, GME'70, an obstetrician-gynecologist; June 11. At the Perelman School of Medicine, Morgan was a member of Alpha Omega Alpha Honor Society, and served his rotating internship and his residency in Obstetrics and Gynecology at the Hospital of the University of Pennsylvania. He also served as a Captain with the U.S. Army Reserve. Morgan was a board-certified diplomate, a fellow of both the American College of Obstetricians and Gynecologists, and the American College of Surgeons; as well as a member of the local, state, and American Medical Societies. He was in private practice in Obstetrics and Gynecology at Mercy Hospital and a member of the Board of Directors of Moses Taylor Hospital, both in Scranton, PA, where he also served as director of Surgery.

David W. Billharz, MD, GME'66, an anesthesiologist; Sept. 22. Billharz graduated from the University of Michigan in 1958 with a pre-med degree and membership in Phi Beta Kappa. He graduated from the State University of New York Downstate Medical School (Brooklyn) in 1962 as a member of the medical honor society, Alpha Omega Alpha. After interning at the Philadelphia Naval Hospital, Billharz completed an anesthesia residency at the Perelman School of Medicine. During his tenure with the U.S. Navy Reserve, Billharz served on the U.S.S. Hospital Ship *Repose* in Vietnam and in various U.S. sites during Desert Storm; after 30 years in the Reserves, he retired as a Captain. Billharz worked with the Associated Anesthesiologists of Reno and upon retiring in

2007, he traveled to Papua New Guinea to spend two months at a mission hospital in Kudjip. Billharz worked for a month on Mercy Ships and spent two months at Tenwek Hospital in Kenya.



Jeffery Hartzell, MD'66, GME'70, a physician; Oct. 13. Hartzell took pre-med classes at Drexel and St. Joseph's Universities before graduating from the Perelman School of Medicine. He worked at Pennsylvania Hospital for more than 30 years, co-founding and serving as first medical director of its groundbreaking hospice care program, and winning the 1998 Jacob Ehrenzeller Award as a distinguished former resident. Hartzell joined a private practice that included former Philadelphia Flyers physician Edward D. Viner and current Flyers medical director Gary W. Dorshimer, serving as team doctor of the Flyers in the 1980s and 1990s. He was also the longtime alternate physician of and traveled overseas with the Philadelphia Orchestra.

1970s

Robert F. Bedford, MD, GME'72, an anesthesiologist; Sept. 2. Bedford received his medical degree from Weill Medical College of Cornell University (New York City). He completed both his residency and fellowship in anesthesiology at the Hospital of the University of Pennsylvania and served as a Major in the Army Medical Corps during the Vietnam War. Bedford spent his career as a clinical professor of Anesthesiology, primarily at the

University of Virginia School of Medicine in Charlottesville. During his career, he served as the chair of Anesthesiology and Critical Care Medicine at Memorial Sloan-Kettering Cancer Center (New York City) and as director of Anesthesia at the U.S. Food and Drug Administration. Bedford also taught anesthesiology at the University of South Florida and was the chief of Anesthesia at the James A. Haley Veterans Administration Hospital, both in Tampa.

Ronald W. Kimball, MD'73, GME'77, an ophthalmologist; Sept. 28. Kimball was a member of the Perelman School of Medicine's Alpha Omega Alpha Honor Medical Society. He completed a residency in ophthalmology at the Scheie Eye Institute. Kimball practiced ophthalmology for 33 years, working in Southwest Philadelphia and performing surgery at the Wills Eye Hospital, Graduate Hospital, and Mercy Fitzgerald Hospital.

Frank C. Passero, MD'73, GME'78, chief of Rheumatology; Aug. 28. After receiving his medical degree from the University of Pennsylvania, Passero completed his internship and medical residency at Pennsylvania Hospital and pursued fellowship training in rheumatology at Penn. He served as chief of Rheumatology at Penn Presbyterian Medical Center and later chief of the Rheumatology Service at Delaware County Memorial Hospital (DCMH, in Drexel Hill), where he also maintained a clinical practice for more than 35 years. Passero was a fellow of the American College of Physicians and of the American College of Rheumatology, as well as a founding fellow of the American Rheumatism Association.

Ralph F. Wetmore Jr., MD'76, GME'81, emeritus professor of Otolaryngology; Sept. 3. Wetmore joined the University of Pennsylvania faculty in 1978 and became a full professor in 2000. Meanwhile, at Children's

Hospital of Philadelphia (CHOP), he treated thousands of children and taught pediatric otolaryngology to medical students, residents, and fellows. Eventually, Wetmore rose to president of the medical staff. He held CHOP's E. Mortimer Newlin Endowed Chair in Pediatric Otolaryngology and Human Communication from 2008 until his retirement in 2020.

1980s

Steven Mark Schreiber, MD'86, an emergency medicine physician; Dec. 23. Schreiber began his 30-year-long career in Wayne (NJ) General Hospital's Emergency Room. He transferred to Pascack Valley Hospital (Westwood, NJ) in 1989; he was the vice chairman of the emergency room and an ACLS/PALS instructor until the hospital's closure in 2007, after which he eventually joined Chilton Hospital (Pompton Plains, NJ). Schreiber retired from his career in emergency medicine in 2016 but continued to work at TKL Research as a principal investigator for medical clinical trials until 2022.

1990s

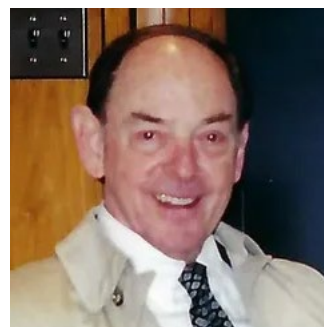
Susan L. Rattner, MD, MSCE'93, an internist; Dec. 22. Rattner attended Columbia University's College of Physicians & Surgeons where she was elected to the medical honor society, Alpha Omega Alpha. She completed a residency in internal medicine at Columbia-Presbyterian Hospital in 1981. Rattner was board certified in internal medicine, joined a faculty practice at Penn Presbyterian Medical Center for the next two years, and then joined the faculty at Hahnemann University in Philadelphia. In 1987, she joined the Dean's Office at Hahnemann as assistant dean for Student Affairs. In 1993, Rattner earned an MS in Clinical Epidemiology from the Perelman

School of Medicine and moved to Jefferson Medical College in 1994.

Rattner continued to practice internal medicine and worked in the Jefferson Dean's office where she rose to become vice dean for Academic Affairs/Undergraduate Medical Education. She was elected to Fellowship in the American College of Physicians in 1999. Rattner was an editor of the book *Professionalism in Medicine: The Case-based Guide for Medical Students*. In 2016, she retired from Jefferson as Professor of Medicine, but continued to care for patients on the physical staff in Women's Health at the Philadelphia VA. Rattner also volunteered in internal medicine at the Community Volunteers in Medicine clinic in West Chester. She was a long-time faculty advisor for the Foundation for the Advancement of International Medical Education and Research.

FACULTY

Arthur K. Asbury, MD, Van Meter Professor of Neurology Emeritus; Oct. 19. Asbury fulfilled his postgraduate training in



medicine, neurology, pathology, and neuropathology at Massachusetts General Hospital and Harvard Medical School, both in Boston. He then became chief of the Neurology Service at the San Francisco Veterans Administration Medical Center in 1969. Concurrently, he was appointed as associate professor and then professor of Neurology and Pathology and vice chair of Neurology

at the Medical School of the University of California, San Francisco.

Asbury was editor-in-chief of the *Annals of Neurology* for eight years. He was a co-editor of the two-volume *Diseases of the Nervous System* and co-editor of the *Blue Books of Practical Neurology*, and served on editorial boards of 11 scientific journals. He also served as the president of the American Neurological Association in 1983.

In 1973, Asbury was selected as chair of Neurology at the University of Pennsylvania School of Medicine. He assumed the role of chair in 1974 and stepped down in 1982. The following year, he was appointed the first Van Meter Professor of Neurology. Asbury was interim dean and executive vice president of the University of Pennsylvania Medical Center from 1988 to 1989. Subsequently, he fulfilled a three-year term as vice dean for Research and a four-year term as vice dean for Faculty Affairs. Asbury again became interim dean of the School of Medicine from 2000 to 2001.

In 2004, the Medical School established the annual Outstanding Faculty Mentoring award in Asbury's name. He received the Penn Medical System's Master Clinician award, the University's Lindback Award for teaching excellence, and in 2015, the University conferred him with the honorary Doctor of Sciences. The department of Neurology launched the Asbury Accelerator Fund in his honor. In 2019, he and his wife of 42 years, Dr. Carolyn Asbury, established the Arthur Knight Asbury, MD Professorship at the Perelman School of Medicine to be held by the Neurology Department Chair, honoring Frances E. Jensen, MD, as the inaugural chair holder in 2021.

Stanley Baum, MD. See Class of 1961.

Robert I. Berkowitz, MD, associate professor of Pediatrics; Oct. 16. Berkowitz earned his medical degree from the University of Connecticut (Farmington) in 1973. He completed his residency



in psychiatry there in 1975, was a fellow at Yale University's Child Study Center until 1977, and worked for a decade as an assistant professor and senior resident in Stanford University's Division of Child Psychiatry and Behavioral Sciences. Berkowitz was the medical director of the Center for Weight and Eating Disorders in the University of Pennsylvania's department of Psychiatry for 25 years, as well as associate professor of Psychiatry and Pediatrics, professor emeritus of continuing education in Psychiatry, and faculty member in the Psychiatry department at Penn Medicine's Abramson Cancer Center. At Children's Hospital of Pennsylvania (CHOP), he was psychiatrist-in-chief and chair of the department of Child and Adolescent Psychiatry, and helped create CHOP's groundbreaking New Jersey Transition to Adult Coordinated Care program that guides families and young patients into adulthood.

Berkowitz co-published *Obesity: A Guide for Mental Health Professionals*, was on the editorial board of the *International Journal of Obesity*, and reviewed articles for the *Journal of Adolescent Health Care* and other publications.

Dwight L. Evans, MD, chair of Psychiatry; Nov. 19. Evans received an MS in Psychology from Bucknell University (Lewisburg, PA) and his medical degree from Temple University. After successfully completing his Psychiatry residency at the University of North Carolina (UNC) Memorial Hospital in Chapel Hill and a fellowship as a Robert Wood Johnson Clinical Scholar, he was appointed to the faculty of the

UNC Department of Psychiatry from 1980 to 1992. Evans completed his psychoanalytic training at the University of North Carolina-Duke University Psychoanalytic Education Program in 1983.

From 1992 to 1997, he served as chair of Psychiatry at the University of Florida (Gainesville), where he also served as director of the Psychoneuroimmunology Laboratory. Evans subsequently served as chair of Psychiatry at



the Perelman School of Medicine, and as the Ruth Meltzer Professor of Psychiatry from 1997 to 2016. In 2015, he was named the inaugural Roehrhoff Rickels Professor of Psychiatry.

He oversaw the establishment of Penn Behavioral Health and served in key leadership roles such as psychiatrist-in-chief of the University of Pennsylvania Health System, director of the Penn Comprehensive Depression Center, and co-director of the Penn Medicine Neuroscience Center. Evans' pioneering translational research on the neurobiology of stress and depression was continuously funded by the NIH for more than 30 years. He also led the creation of the NIH-funded Penn Mental Health AIDS Research Center and served as its director.

Evans received the Award for Research in Psychiatry from the American Psychiatric Association and the William C. Menninger Memorial Award for Distinguished Contributions to the Science of Mental Health from the American College of Physicians. He served as president of the American College of Psychiatrists and the American Foundation for Suicide Prevention (AFSP) as well as on numerous

boards, including the National Network of Depression Centers, the American Psychiatric Association (APA) Foundation, and the APA Council on Research. Evans published extensively, including a clinician's guide to treating and preventing adolescent mental health disorders, which was awarded "Best Book in Clinical Medicine" by the Association of American Publishers.

Samuel G. Jacobson, MD, William C. Frayer Professor of Ophthalmology; Jan. 4. Jacobson received his medical degree from the University of Illinois and his PhD from the University of London (UK), completed residencies at Massachusetts Eye and Ear (Boston) and Rush Presbyterian (Chicago), and held fellowships at Mass Eye and Ear and Moorfields Eye Hospital (London, UK). In 1995, he founded and directed the Center for Hereditary Retinal Degenerations at Scheie Eye Institute. Prior to this, Jacobson had served on the faculty of Bascom Palmer Eye Institute at the University of Miami for 12 years, where he established the Institute's first program for inherited retinal degenerations.

Jacobson was a co-recipient of the Antonio Champalimaud Vision Award in 2018 for his revolutionary work that led to the first gene therapy approved by the FDA for the eye or any inherited condition. In 2018, he was awarded the ARVO Proctor Medal for his research with colleague Artur Cideciyan, PhD. In 2023, Jacobson was selected as a co-recipient of the Helen Keller Prize for Vision Research.

Frank C. Passero, MD. See Class of 1973.

William H. Simon, MD. See Class of 1963.

Edward J. Stemmler, MD. See Class of 1960.

Robert E. Weibel, MD. See Class of 1955.

Ralph F. Wetmore Jr., MD. See Class of 1976.

Greater Benefit, Greater Impact



*A win-win situation.
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A wonderful way to
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and to extend our gratitude.*

Many Penn Medicine donors have shared over the years how legacy giving fits well into their financial planning and supports their vision for lasting personal impact. In addition to helping further growth and progress at Penn, donors have been motivated by significant financial benefits such as tax deductions and partially tax-free lifetime payments. Now, thanks to legislation passed in December 2022 — known collectively as "Secure 2.0" — it's even easier to satisfy the desire to give while also enhancing your own financial future.

"The intent of the Act is right in the name: 'Setting Every Community Up for Retirement Enhancement,'" said Scott Harkey, Director of Development. "We're excited to be able to offer this new option to our donors and alumni because it could make your charitable giving in retirement more tax-efficient."

One key change gives retirees more time to save and enjoy additional tax-free growth — and allows stock portfolios to recover in an unsettled economic climate. **By increasing the age at which retirees must begin taking taxable withdrawals** from 72 to 73 in 2023, and to 75 by 2033, Secure 2.0 allows donors to be in a better financial position to create their legacy through philanthropic giving.

Another change Secure 2.0 brings is **the ability to distribute from an IRA to fund a life income gift**, which allows you to make a gift to a qualified charitable organization and receive lifetime payments to boost your retirement income or provide a lifetime payment for you or your spouse. Retirees 70½ or older can fund a charitable gift annuity, charitable remainder unitrust, or charitable remainder annuity trust by making a one-time election for a qualified charitable distribution of up to \$50,000 from an IRA during a single calendar year without being taxed on the distribution. This opportunity comes with special rules, so contact Penn Medicine to see if it is right for you.

Also, beginning in 2024, **the annual limit on direct gifts to qualified charities from an IRA will be adjusted annually for inflation**, which allows donor generosity to keep pace with economic shifts. Currently, those 70½ or older can give up to \$100,000 to a qualified charity directly from their IRA without paying income taxes on the distribution.

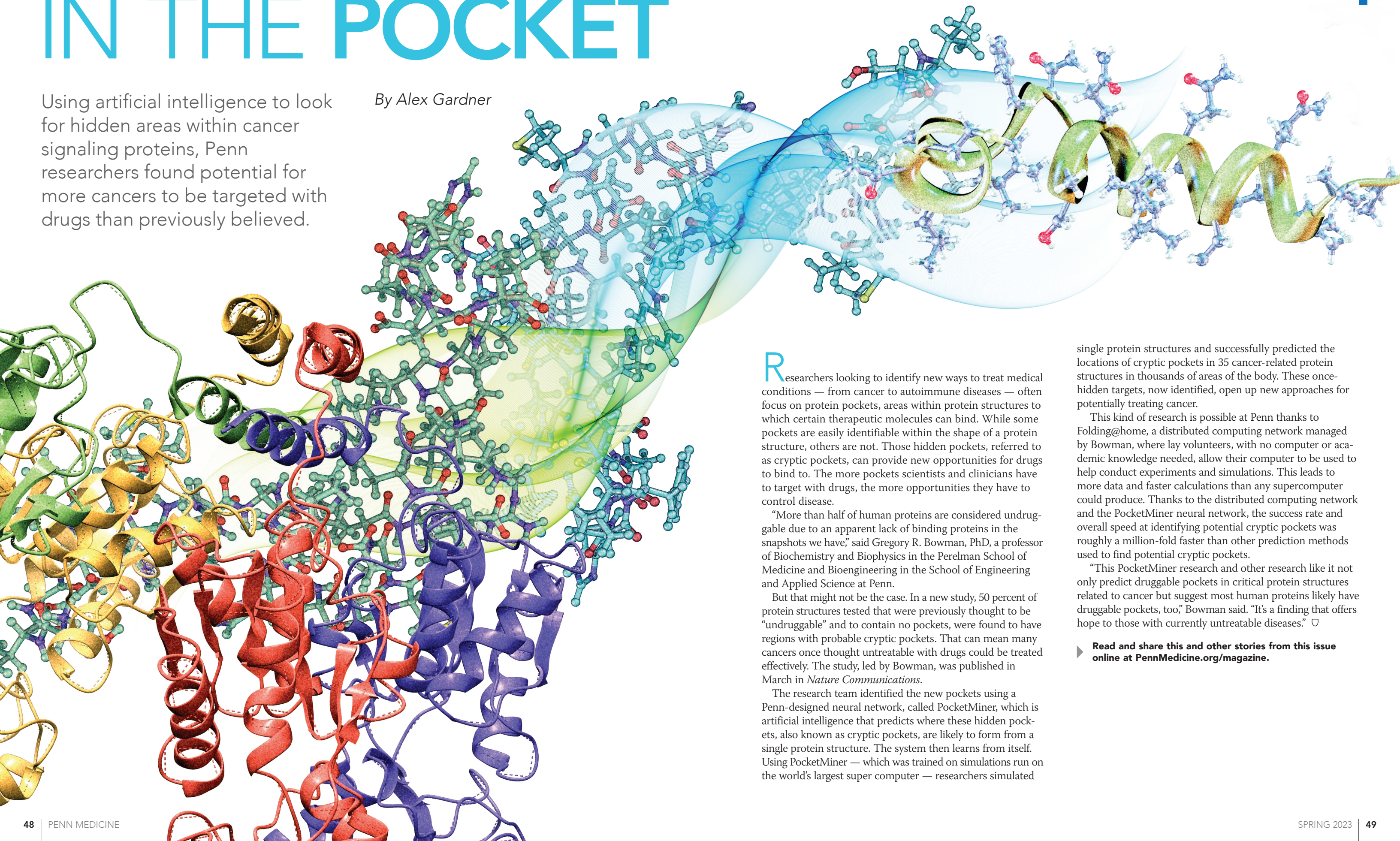
► **For more information, please visit our website at: www.pennmedicine.org/plannedgiving.**

If you have any questions about how the new retirement laws could maximize your charitable giving to Penn Medicine, talk to your financial advisor or reach out to Scott Harkey at harkeys@upenn.edu or 215-284-6266.

IN THE POCKET

Using artificial intelligence to look for hidden areas within cancer signaling proteins, Penn researchers found potential for more cancers to be targeted with drugs than previously believed.

By Alex Gardner



Researchers looking to identify new ways to treat medical conditions — from cancer to autoimmune diseases — often focus on protein pockets, areas within protein structures to which certain therapeutic molecules can bind. While some pockets are easily identifiable within the shape of a protein structure, others are not. Those hidden pockets, referred to as cryptic pockets, can provide new opportunities for drugs to bind to. The more pockets scientists and clinicians have to target with drugs, the more opportunities they have to control disease.

“More than half of human proteins are considered undruggable due to an apparent lack of binding proteins in the snapshots we have,” said Gregory R. Bowman, PhD, a professor of Biochemistry and Biophysics in the Perelman School of Medicine and Bioengineering in the School of Engineering and Applied Science at Penn.

But that might not be the case. In a new study, 50 percent of protein structures tested that were previously thought to be “undruggable” and to contain no pockets, were found to have regions with probable cryptic pockets. That can mean many cancers once thought untreatable with drugs could be treated effectively. The study, led by Bowman, was published in March in *Nature Communications*.

The research team identified the new pockets using a Penn-designed neural network, called PocketMiner, which is artificial intelligence that predicts where these hidden pockets, also known as cryptic pockets, are likely to form from a single protein structure. The system then learns from itself. Using PocketMiner — which was trained on simulations run on the world’s largest super computer — researchers simulated

single protein structures and successfully predicted the locations of cryptic pockets in 35 cancer-related protein structures in thousands of areas of the body. These once-hidden targets, now identified, open up new approaches for potentially treating cancer.

This kind of research is possible at Penn thanks to Folding@home, a distributed computing network managed by Bowman, where lay volunteers, with no computer or academic knowledge needed, allow their computer to be used to help conduct experiments and simulations. This leads to more data and faster calculations than any supercomputer could produce. Thanks to the distributed computing network and the PocketMiner neural network, the success rate and overall speed at identifying potential cryptic pockets was roughly a million-fold faster than other prediction methods used to find potential cryptic pockets.

“This PocketMiner research and other research like it not only predict druggable pockets in critical protein structures related to cancer but suggest most human proteins likely have druggable pockets, too,” Bowman said. “It’s a finding that offers hope to those with currently untreatable diseases.” □

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THE FIRST WAVE OF A REVOLUTION WAS 'A 20-YEAR OVERNIGHT SENSATION'

The crowd that gathered on August 30, 2017, at the Perelman Center for Advanced Medicine, had a lot to celebrate. That day, the U.S. Food and Drug Administration officially approved a Penn Medicine-developed personalized cellular immune therapy — one that changed the landscape of cancer care. But it was only one part of a larger story that is still unfolding. Since that fateful day, dozens more drugs and devices rooted in research at Penn have achieved FDA approval, for reasons that are a lot more than luck. Science has shifted toward more discoveries based on the underlying mechanism of disease, especially in cancer. Through a particularly robust clinical trial and commercialization infrastructure, Penn has further worked to smooth every part of the path from idea to implementation. And to ensure that state-of-the-art treatments reach the patients who need them, Penn Medicine teams have also kept focus on equity and access during clinical trials and after therapies are approved.

▶ [Read more on page 14.](#)

